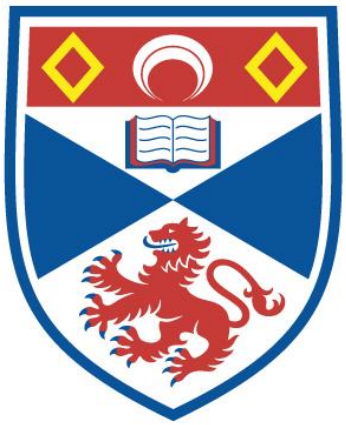
SYNTHESIS AND REACTIVITY STUDIES OF MONO- AND DIAURATED SPECIES BEARING N-HETEROCYCLIC CARBENE LIGANDS

Adrián Gómez Suárez

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



2014

Synthesis and Reactivity Studies of Mono- and Diaurated Species Bearing *N*-Heterocyclic Carbene ligands

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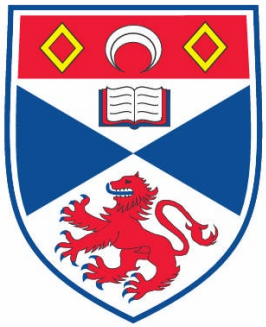

This thesis is submitted in partial fulfilment for the degree of PhD

at the

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09 July 2014

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"I'm Mad Al, he's Sane Alex, and that's Adrian, who says he's not mad but can't prove it"

Terry Pratchett, *Going Postal*

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The wonderful journey that has been my PhD started almost four years ago. The path was not always clear or easy to walk but I had amazing people at my side that made it possible. I am well aware that without their help and support I would not be here today, therefore credit should be given to those who deserve it.

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Author Contributions

The majority of the work reported in this thesis has been published as peer-reviewed journal articles as described below. Unless stated otherwise, the work reported is all my own work and I was the primary researcher on all projects and prepared all published manuscripts:

Chapter 1:

- Adapted with permission from *"Dinuclear Gold Catalysis: Are Two Gold Centers Better than One?",* Gómez-Suárez, A.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2012**, *51*, 8156. Copyright© 2012 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

Chapter 2:

- Adapted with permission from *"Influence of a Very Bulky N-Heterocyclic Carbene in Gold-Mediated Catalysis",* Gómez-Suárez, A.; Ramón, R. S.; Songis, O.; Slawin, A. M. Z.; Cazin, C. S. J.; Nolan, S. P.*, Organometallics* **2011**, *30*, 5463. Copyright© 2011 American Chemical Society.

R. S. Ramón contributed with preliminary synthetic results, helpful suggestions and proof reading of the manuscript. O. Songis contributed with the synthesis of [Cu(IPr*)Cl]. A. M. Z. Slawin carried out the X-ray diffraction analyses.

Chapter 3:

- Adapted with permission of The Royal Society of Chemistry from *"Straightforward Synthesis of [Au(NHC)X] (NHC = N-Heterocyclic Carbene, X = Cl, Br, I) Complexes",* Collado, A.; Gómez-Suárez, A.; Martin, A. R.; Slawin, A. M. Z.; Nolan, S. P.*, Chem. Commun.* **2013**, *49*, 5541.

A. Collado carried out significant amount of experimental work and was the author of the manuscript. Therefore, Chapter 3 was largely rewritten. A. R. Martin provided IPr*^{Tol}•HCl. A. M. Z. Slawin carried out the X-ray diffraction analyses.

Chapter 4:

- Adapted with permission of The Royal Society of Chemistry from *"Synthetic Routes to [Au(NHC)(OH)] (NHC = N-Heterocyclic Carbene) Complexes",* Gómez-Suárez, A.; Ramón, R. S.; Slawin, A. M. Z.; Nolan, S. P.*, Dalton Trans.* **2012**, *41*, 5461.

R. S. Ramón contributed with preliminary synthetic results, helpful suggestions and proof reading of the manuscript. A. M. Z. Slawin carried out the X-ray diffraction analyses.

- And, a small part adapted with permission from *"New [Au(NHC)(OH)] Complexes for Silver-Free Protocols"*, *Organometallics* **2013**, *33*, 421.Patrick, S. R.; Gómez-Suárez, A.; Slawin, A. M. Z.; Nolan, S. P. Copyright© 2013 American Chemical Society.

Chapter 5:

- Adapted with permission from *"[{Au(NHC)}$_2$(μ-OH)][BF$_4$]: Silver-Free and Acid-Free Catalysts for Water-Inclusive Gold-Mediated Organic Transformations",* Gómez-Suárez, A.; Oonishi, Y.; Meiries, S.; Nolan, S. P.*, Organometallics*, **2013**, *32*, 1106. Copyright© 2013 American Chemical Society.

Y. Oonishi contributed with some of the catalytic experiments, helpful suggestions and proof reading of the manuscript. S. Meiries provided IPent•HCl.

Chapter 6:

- Adapted with permission from *"Straightforward Synthetic Access to gem-Diaurated and Digold σ,π-Acetylide Species",* Gómez-Suárez, A.; Dupuy, S.; Slawin, A. M. Z.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2013**, *52*, 938. Copyright© 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

S. Dupuy contributed almost equally to the experimental work. A. M. Z. Slawin carried out the X-ray diffraction analysis.

Chapter 7:

- Adapted with permission from *"Hydrophenoxylation of Alkynes by Cooperative Gold Catalysis",* Oonishi, Y.; Gómez-Suárez, A.; Martin, A. R.; Nolan, S. P.*, Angew. Chem. Int. Ed.* **2013**, *52*, 9767; and some unpublished results. Copyright© 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

Y. Oonishi and A. R. Martin contributed by carrying out part of the reaction scope, as well as helpful suggestions and proof reading of the manuscript.

Several articles were also published during the course of my PhD as a result of collaborative efforts but have not been included in this thesis:

- *"Gold(I)-Catalysed Tandem Alkoxylation/Lactonization of γ-Hydroxy-α,β-Acetylenic Esters",* Ramón, R. S.; Pottier, C.; Gómez-Suárez, A.; Nolan, S. P., *Adv. Synth. Catal.* **2011**, *353*, 1575.
- *"Synthesis, Characterisation, and Oxygen Atom Transfer Reactions Involving the First Gold(I)-Alkylperoxo Complexes",* Collado, A.; Gómez-Suárez, A.; Slawin, A. M. Z.; Nolan, S. P., *Chem. Commun.* **2013**, *49*, 10745.

- *"Synthesis, Characterization and Luminiscence Studies of Gold(I)-NHC amide Complexes",* Gómez-Suárez, A.; Nelson, D. J.; Thompson, D. G.; Cordes, D. B.; Graham, D.; Slawin, A. M. Z.; Nolan, S. P., *Beilstein J. Org. Chem.* **2013,** *9,* 2216.

Table of Contents

Abbreviations

Å	angstrom
Anal. calcd	analysis calculated
Ar	aryl
aq.	Aqueous
Bu	butyl
^{t}Bu	*tert*-butyl
CAAC	cyclic alkyl amino carbene
d	doublet
DCE	1,2-dichloroethane
DCM	dichloromethane
DFT	density functional theory
Dipp	2,6-di*iso*propylphenyl
DMF	dimethylformamide
DMSO	dimethylsulfoxide
eq.	equation
equiv.	equivalent
Et	ethyl
exc.	excess
g	grams
GC	gas chromatography
h	hours
Hex	hexyl
HSAB	hard/soft acid/base
IAd	1,3-bis(adamantyl)imidazol-2-ylidene
I^{t}Bu	1,3-bis(*tert*-butyl)imidazol-2-ylidene
ICy	1,3-bis(cyclohexyl)imidazol-2-ylidene
IDD	1,3-bis(cyclododecyl)imidazol-2-ylidene
IMes	1,3-bis(mesityl)imidazol-2-ylidene
IPent	1,3-bis(2,6-bis(1-ethylpropyl)phenyl)imidazol-2-ylidene
IPr	1,3-bis(2,6-di*iso*propylphenyl)imidazol-2-ylidene
IPr^{Cl}	4,5-dichloro-1,3-bis(2,6-di*iso*propylphenyl)imidazol-2-ylidene
IPr^{Me}	4,5-dimethyl-1,3-bis(2,6-di*iso*propylphenyl)imidazol-2-ylidene
IPr*	1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazol-2-ylidene

IPr*$^{-Tol}$	1,3-bis(2,6- bis(di-*p*-tolylmethyl)-4-methylphenyl)imidazol-2-ylidene
IsB	1,3-bis(*iso*butyl)imidazol-2-ylidene
JohnPhos	(2-Biphenyl)di-*tert*-butylphosphine
L	neutral ligand
LTM	late transition metal
m	*meta*
Me	methyl
Mes	mesityl
mg	milligrams
MHz	megahertz
min	minutes
mL	millilitres
μL	microliters
mmol	millimoles
μmol	micromoles
mol	moles
mol%	molar percentage
MW	microwave
M	metal
NMR	nuclear magnetic resonance
NHC	*N*-heterocyclic carbene
o	*ortho*
p	*para*
Ph	phenyl
Pht	phtalimide
PPh_3	triphenylphosphine
ppm	parts per million
q	quartet
R	alkyl group
RT	room temperature
s	singlet
satd.	Saturated
SIMes	1,3-bis(mesityl)imidazolin-2-ylidene
SIPr	1,3-bis(2,6-di*iso*propylphenyl)imidazolin-2-ylidene
SITb	1,3-bis(3,5-di*tert*-butylphenyl)imidazolin-2-ylidene
t	triplet

THF	tetrahydrofuran
tht	tetrahydrothiophene
Xphos	2-Dicyclohexylphosphino-2′,4′,6′-tri*iso*propylbiphenyl

Abstract

The use of Au-NHC complexes in homogenous gold catalysis has become very popular during the last 10 years. The work described in this thesis represents a modest contribution towards a better understanding of the reactivity of these fascinating complexes and the intermediate species involved during gold-catalysed transformations.

There are two main themes that permeate the following chapters: a) synthesis and reactivity studies of monoaurated species and b) synthesis and reactivity studies of diaurated species.

The main motivation for the work presented herein was to develop more efficient synthetic routes towards a series of gold complexes, such as [Au(NHC)Cl], [Au(NHC)(OH)] and [{Au(IPr)}$_2$(μ-OH)][X], in order to be able to further explore their reactivity.

Chapter 2 constitutes the first approach that I had with the chemistry of Au-NHC complexes, and describes our efforts to evaluate how the use of a highly sterically demanding NHC ligand affects gold-catalysed transformations.

Chapters 3 and 4 explore alternative, more efficient synthetic routes towards known Au-NHC complexes. For example, a new, highly robust protocol has been developed for the synthesis of [Au(NHC)X] (X = Cl, Br, I) complexes, which are the starting materials to prepare a wide range of Au-NHC based species. Moreover, as a result of our investigations it has been possible to isolate a series of [Au(NHC)(OH)] species and to gain some insight into the stability of these complexes.

Chapters 5 and 6 describe the synthesis and applications of digold hydroxide species [{Au(IPr)}$_2$(μ-OH)][X] in a series of catalytic and stoichiometric transformations. For example, they have been used as silver-free catalysts for water-inclusive gold-catalysed transformations or to access key intermediates in gold catalysis, such as *gem*-diaurated and σ,π-digold-acetylide species.

Finally, Chapter 7 combines what we learned about the reactivity of [{Au(IPr)}$_2$(μ-OH)][X] in order to develop for the first time a gold-catalysed transformation where *two* gold centres independently react with *two* substrate molecules to catalyse the hydrophenoxylation of alkynes.

1. General Introduction

1.1 Gold in Homogeneous Catalysis

The end of the 20th century and the beginning of the 21st flooded the chemistry world with a "*gold rush*";[1] this has resulted in an exponential growth on the number of publications dealing with the reactivity of this precious metal, both in stoichiometric and catalytic fashions, during the last decade.[2] The main driving force of this modern gold fever was the discovery that, despite being considered as inert catalytic species for a long time, gold salts/complexes could catalyse a wide range of chemical reactions.[2] Initially, these catalytic transformations were carried out using simple Au^{I}/Au^{III} salts, such as AuCl, $AuCl_3$ or $X[AuCl_4]$ ($X = Na^+$, NH_4^+, etc.). However, scientists rapidly realised that the use of ancillary ligands helped to stabilise the proposed active species $[Au]^+$. Therefore, phosphine gold complexes $[Au(PR_3)X]$ (X = Me, Cl), which had been known for a long time,[3] rapidly became ubiquitous in literature reports. Moreover, since the blossoming of *N*-heterocyclic carbenes (NHC) as ancillary ligands for transition metal complexes,[4] [Au(NHC)Cl] species have become rather popular in gold catalysis.[5]

Since the beginning, the majority of gold-catalysed transformations took advantage of the exceptional Lewis acidity displayed by gold species to activate C-C multiple bonds, generally alkynes, towards nucleophilic attacks.[6] In order to gain a better understanding about *why* gold displays such an exceptional Lewis acid character it is necessary to focus on the relativistic effects that affect this precious metal. Although such effects are present in many heavy elements, gold is the atom where they are more pronounced and thus most strongly influence properties. These relativistic effects account for the high electronegativity and electron affinity of gold, its high ionisation potentials and some of its physical properties.

1.1.1 *Relativistic Effects on Gold*

The following will be a brief summary of the relativistic effects affecting gold species. This is a very complex phenomenon that would require a separate discussion on the field of quantum physics, which is not the main focus of this thesis. For further details see a Pyykkö's review "*Theoretical Chemistry of Gold*".[7]

The term "relativistic effects" refers to any phenomenon resulting from the need to consider velocity (υ) as significant relative to the speed of light (c) in equation 1, where m is relativistic mass and m_0 is non-relativistic mass.[2i,7-8]

$$m = \frac{m_0}{\sqrt{1-(v/c)^2}} \qquad (1)$$

For a given atom, the average radial velocity of the 1s electrons is $\upsilon_r = Z$. This means that for elements with atomic number $Z > 70$, the mass of the 1s electrons significantly increases. As the Bohr radius is inversely related to the mass of the electron, this increase in mass corresponds to a decrease in radius. This relativistic contraction can be extrapolated to all other *s* and *p* orbitals. Therefore, the electrons are closer to the nucleus and have greater ionisation energies. In addition, the contraction of the 6*s* orbital leads to the shielding of the 4*f* and 5*d* filled orbitals, thus reducing the nuclear attraction and resulting in the expansion of these orbitals (Figure 1).[2i,7-8] In addition, also as a consequence of a relativistic treatment, spin-orbit coupling is observed which accounts for the splitting of the 5*d* orbitals (Figure 1).[2i,7-8]

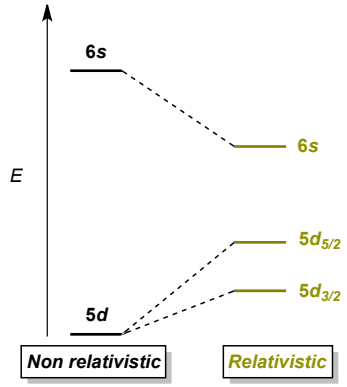


Figure 1. Contraction of 6*s* orbital and expansion of 5*d* orbitals due to relativistic effects in Au^I

The contraction of the 6*s* orbital leaves the lowest unoccupied molecular orbital (LUMO) for Au^I species in a low energy level in comparison to other metals of the same group, thus it is responsible for its higher Lewis acidity. Therefore, gold(I) complexes can be considered as extremely soft Lewis acids, which would preferentially interact with soft nucleophiles such as π C-C bonds, e.g. alkynes. This would explain the carbophilicity of Au^I complexes and its high affinity towards C-C multiple bonds.

Some physical properties of gold can also be explained through relativistic effects. For example, its yellow colour can be rationalised due to the decrease in the band gap between the 5*d* (HOMO) and 6*s* (LUMO) orbitals, which results in an electronic transition in the visible spectrum.[2i,7-8] Moreover, another consequence of the contraction of the *s* orbitals due to relativistic effects is the significantly smaller atomic radius of gold in comparison with silver (135 pm *vs.* 160 pm).[2i,7-8]

The relativistic effects can also be used to explain why higher oxidation states are accessible for Au in comparison to Cu and Ag. While the first ionization potential is rather high for Au, due to the contraction of the 6*s* orbital, the second and third ionization potentials are significantly lower as the electrons are in more accessible, energetically-higher 5*d*

orbitals. Since the 5*d* and 6*s* orbitals are separated by a small energy gap, which allows the formation of hybrid orbitals that are suitable for the formation of strong bonds in square planar configurations, the Au^{III} oxidation state is stabilised.[2i,7-8] However, although Au^{III} is easily accessible, gold complexes do not usually switch between oxidation states in catalysis without the use of an additional oxidant. Gold(III) has also found catalytic applications, however it can be considered as a harder Lewis acid than gold(I), thus displaying a more oxophilic rather than carbophilic character.[2i,7-8]

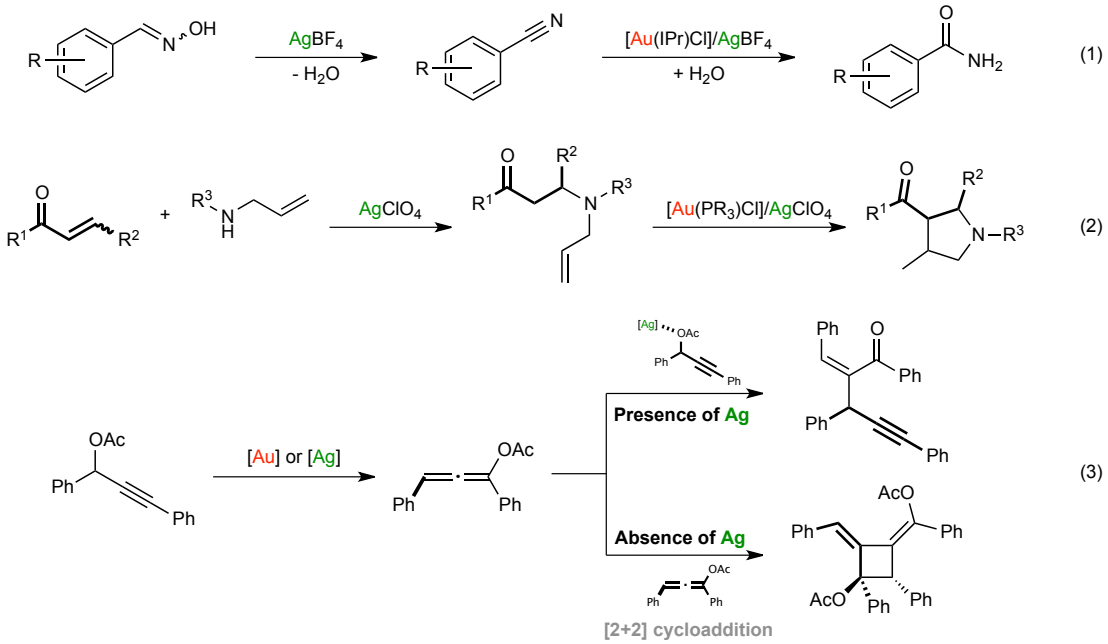
Another characteristic property of gold that can be attributed to relativistic effects is the so-called "*aurophilicity*": the tendency of gold(I) complexes to aggregate through formation of Au-Au interactions similar to hydrogen bonding.[2g,2h,9] This type of attractions were summarised by Schmidbaur as *"In high-level theoretical treatments the attraction is rationalized as a ''super van der Waals bonding'' based on particularly strong relativistic, dispersion and correlation effects"*.[2h]

In summary, the exceptional reactivity presented by gold can be viewed as a direct consequence of the relativistic effects that affect this precious metal and influence its catalytic behaviour.

1.1.2 *Silver Effect and Silver-Free Protocols for Gold Catalysis*

With the advent of the 21st century and the subsequent "*gold rush*" a new era began in gold catalysis.[1,2f] Simple gold salts, such as AuCl or $AuCl_3$, slowly started to give way to more sophisticated organogold complexes, such as [Au(L)Cl] (L = PR_3 or NHC), that enhanced the stability of the catalytically active species $[Au(L)]^+$. However, one common theme remained untouched: the addition of a halogen scavenger to generate the active species. Due to their effectiveness at this task, the use of silver salts as halogen abstractors became ubiquitous in gold catalysis. However, as silver itself could be catalytically active,[10] silver salts are far from being mere spectators in gold-catalysed reactions. Several research groups have reported catalytic protocols where both [Ag] and [Au] are necessary in order to achieve the desired products (Scheme 1). For example, in 2010 our group reported the Au/Ag co-catalysed rearrangement of aldoximes to amides (eq. 1, Scheme 1).[11] It was proposed that $AgBF_4$ would act as both a catalyst, to form nitriles from aldoximes, and a halogen scavenger, to activate [Au(IPr)Cl] that would catalyse the hydration of nitriles to form amides.[11] One year later, Che and co-workers reported another example of a Au/Ag co-catalysed reaction (eq. 2, Scheme 1).[12] In this case, $AgClO_4$ would catalyse the *N*-Michael addition of allylic amines to α,β-unsaturated ketones, while $[Au(PR_3)Cl]$ would catalyse an intramolecular hydroalkylation to form the desired pyrrolidine derivative.[12] Shi and co-workers have recently reported the gold-catalysed rearrangement of propargylic esters and how the subsequent reactivity depends on the presence or absence of silver salts (eq. 3, Scheme 1).[13] When the

reaction was carried out in the presence of AgOTf, the dimerisation of the starting material was observed as the main process, while when the reaction was performed in the absence of AgOTf a cyclobutane derivative was obtained.[13]



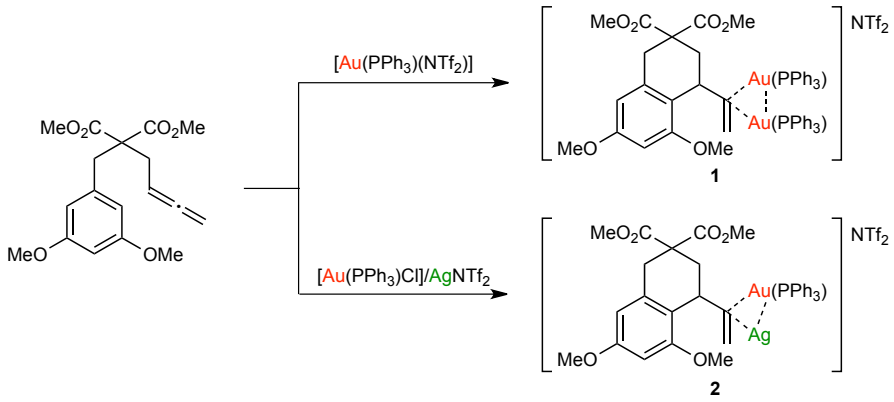
Scheme 1. Selected examples of Au/Ag co-catalysed reactions

Due to the ability of silver salts to catalyse certain organic transformations, it is a common practice to test whether they can catalyse the targeted reaction in the absence of gold. However, even if the catalyst screening reveals that silver salts are unable to catalyse a given reaction, this does not mean that they cannot interfere somehow with the gold catalyst. The possibility that silver salts could be more than mere spectators in gold catalysis has encouraged several research groups to investigate this so called "*silver effect*".

1.1.2.1 Silver Effect in Gold Catalysis

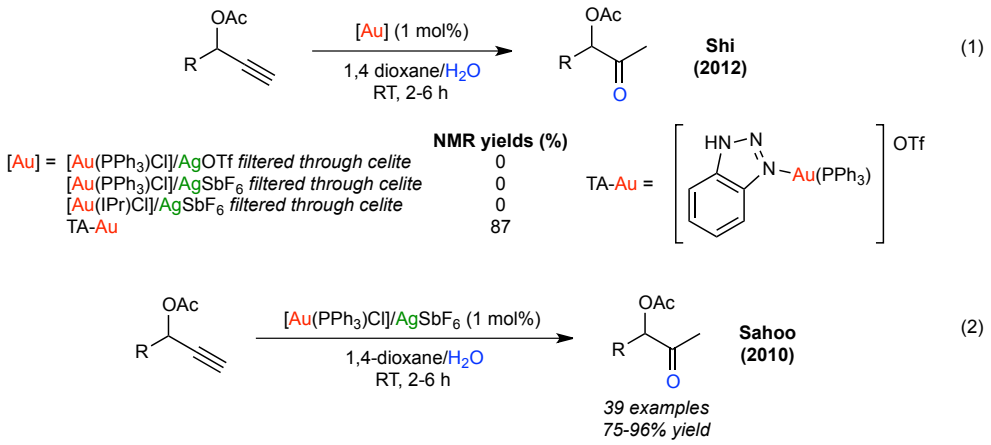
Despite the general use of silver salts in gold catalysis, studies about their interactions with gold complexes are relatively new and scarce. Gagné and co-workers reported the first study on the silver effect in gold catalysis in 2009 (Scheme 2).[14] Through a series of NMR experiments they observed different catalyst resting states when they were working in the presence or absence of silver salts. If the reaction was carried out using $[Au(PPh_3)(NTf_2)]$ the resting state was a *gem*-diaurated species (**1**).[14] However, if a mixture of $[Au(PPh_3)Cl]/AgNTf_2$ was employed, different ^{1}H and $^{31}P\{^{1}H\}$ spectra were observed. The ^{1}H NMR spectrum revealed a 1:1 ratio between the PPh_3 signals of the gold complex and the organic substrate, which in combination with high resolution mass spectroscopy analyses, led them to propose a Au/Ag bimetallic resting state (**2**).[14] In addition, they proved that **1** could

be converted to **2** by addition of 3 equiv. of $AgNTf_2$. The effect of this excess silver on the reaction kinetics was also investigated; if a 3-fold excess of $AgNTf_2$ was employed, with respect to the gold, the reaction rate decreased significantly compared to the silver free reaction.[14] In summary, this study showed how the presence of silver salts can influence catalyst resting states and reaction kinetics in gold-catalysed processes.



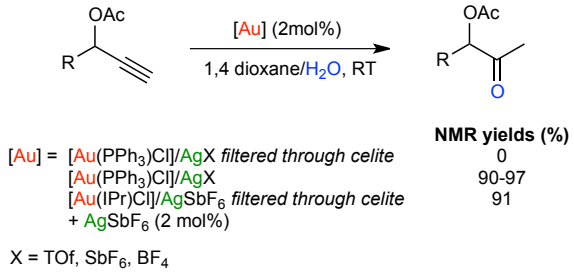
Scheme 2. Difference catalyst's resting states observed by Gagné and co-workers

No further studies were disclosed until 2012, when Shi and co-workers published their controversial study on the silver effect in gold catalysis.[15] They began their investigations by studying the gold-catalysed hydration of propargylic acetates to form α-hydroxy ketones. During the catalyst screening, it was observed that the only active species for this reaction was Shi's triazole-gold complex TA-Au (eq. 1, Scheme 3).[16] Interestingly, these results were in direct contradiction with the work reported by Sahoo in 2010, where a mixture of $[Au(PPh)_3Cl]/AgSbF_6$ was used to catalyse the same transformation (eq. 2, Scheme 3).[17] The main difference between the two procedures was that while the latter mixed all the reagents and activated the catalyst *in situ*; Shi first added the silver salt to a solution of the gold complex, filtered it through a pad of Celite and then added the reagents.



Scheme 3. Difference in reactivity observed by Shi and Sahoo.

Despite the clear difference in experimental procedure, Shi and co-workers proposed that the silver salt was somehow enhancing the catalytic activity of the gold complex. In order to support their claim they ran a series of catalytic tests comparing *in situ* activated catalysts with mixtures of Au/Ag filtered through Celite (Scheme 4). The latter proved to be completely inactive while the *in situ* activated catalysts performed well. However, if an additional amount of silver salt was added to the Au/Ag mixture filtered through Celite, the catalytic activity was restored and excellent conversions were observed. These results prompted Shi and co-workers to suggest that in the case of Sahoo's protocol the active catalyst was a combination of Au/Ag rather than gold alone and encouraged them to study whether this phenomenon was common for other gold-catalysed reactions.[15]



Scheme 4. Comparison of Au/Ag mixtures with and without Celite filtration

Further studies led Shi and co-workers to classify gold-catalysed transformations in three main categories (Figure 2): a) genuine gold catalysis, where there is no difference between filtering the Au/Ag mixture through Celite or not; b) Au/Ag bimetallic catalysis, where higher conversions were achieved through a combination of both metals; and c) silver-assisted gold catalysis, where the reactions can be promoted by either gold, silver, or a combination of both.

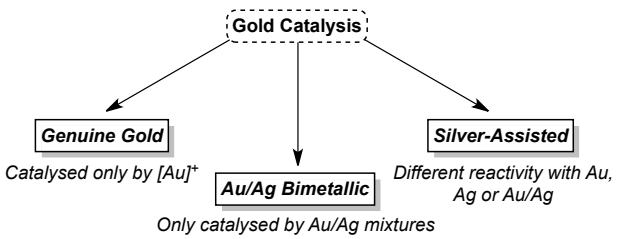


Figure 2. Types of gold-catalysed reactions according to Shi and co-workers

Despite being an interesting study, Shi and co-workers made a series of naïve assumptions that weakened their conclusions:

- They did not provide any data about the amount of catalyst present in solution after the Au/Ag mixture was filtered through Celite. Therefore, the lack of reactivity

observed in these cases could be explained by incomplete chloride abstraction by the silver salts or by loss of catalyst during the filtration.

- If gold complexes and silver salts (with non-coordinating anions) are mixed in the absence of organic substrates or coordinating solvents, this may lead to the formation of catalytically inactive complexes or decomposition of the catalysts. To the best of our knowledge, species of the formula [Au(L)][X] (L = PR_3 or NHC; X = non-coordinating anion) are unstable and examples of such complexes have yet to be isolated.

Regarding the first point, Jones[18] and Echavarren[19] have recently, independently, reported studies on the chloride abstraction from gold complexes using silver salts. Both groups have observed the formation of chloride-bridged dinuclear gold complexes upon reaction of [Au(JonhPhos)Cl] with several silver salts (Figure 3).

After analysing a series of Celite filtered mixtures of [Au(JonhPhos)Cl]/$AgSbF_6$ by elemental analyses, Jones observed that the ratio Au:Ag decreased with longer reaction times (form 1:1 after 30 s to 1:0.06 after 20 h).[18] This suggests that the halogen abstraction is not as efficient or fast as once thought. Moreover, Echavarren performed a series of catalytic studies using the isolated chloride-bridged species. They observed that the chloride-bridged digold complexes were substantially less reactive than their mononuclear, cationic counterparts.[19]

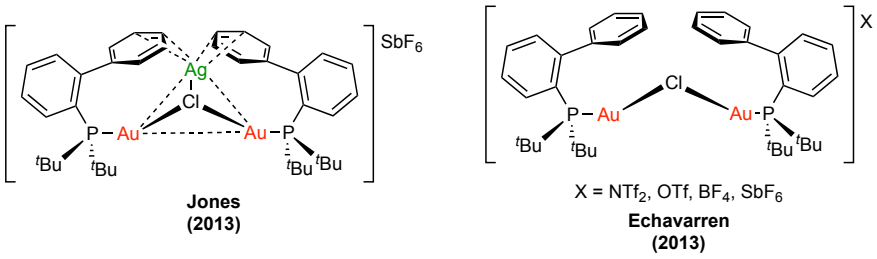


Figure 3. Chloride-bridged dinuclear gold species isolated by Jones and Echavarren

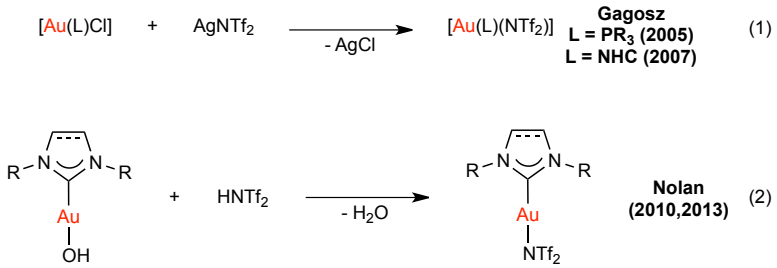
In addition to the studies performed by Jones and Echavarren, Hammond and co-workers have recently reported that the active cationic gold species $[Au(L)]^+$ can be poisoned by the presence of halide or base impurities in the reaction media, thus reducing the reaction conversions.[20] Gratifyingly, they found a possible solution for this problem: the addition of acid activators (e.g. AgOTf, $In(OTf)_3$, HOTf) as sacrificial reagents which bind to the catalyst poison, thus regenerating the active species.[20] They also suggest that the lack of reactivity observed by Shi might be explained by poisoning of the catalyst with basic impurities from the Celite. The addition of an acidic activator, such as AgOTf, would then regenerate the active species.[20]

To avoid problems derived from the use of silver salts, chemists have developed new gold complexes and procedures that remove the need for such additives. The following pages summarise the most common and practical *silver free* protocols for gold catalysis. For further details see a comprehensive review on this topic published by Schmidbaur in 2010.[21]

1.1.2.2 Silver Free Protocols for Gold Catalysis

❖ **[Au(L)(NTf$_2$)] (L = PR$_3$ or NHC) complexes**

Gold complexes of the formula [Au(L)(NTf$_2$)], which are air and moisture stable, base their reactivity on the ability of the triflimide counterion to be displaced by a suitable organic substrate. These complexes are the most common silver free catalysts nowadays, and have proven to be highly active in a wide range of transformations. Moreover, several of them, such as [Au(PPh$_3$)(NTf$_2$)] or [Au(IPr)(NTf$_2$)], are commercially available. Gold-triflimide complexes, bearing either phosphine or NHC ligands, were first reported by Gagosz.[22] They can be easily synthesised by reacting [Au(L)Cl] with AgNTf$_2$, which can be prepared from Ag$_2$CO$_3$ and HNTf$_2$ (eq. 1, Scheme 5).[22] Special care should be taken to ensure complete removal of silver impurities from the isolated complex, as traces of AgNTf$_2$ can influence the reactivity of the catalyst, as noted by Sheppard and co-workers (See Chapter 5 for further details). In order to avoid such problems, our group has recently reported an alternative protocol for the synthesis of [Au(NHC)(NTf$_2$)].[23] This kind of complex can be easily synthesised from [Au(NHC)(OH)] and HNTf$_2$, producing water as the sole by-product of the reaction (eq. 2, Scheme 5).[23]



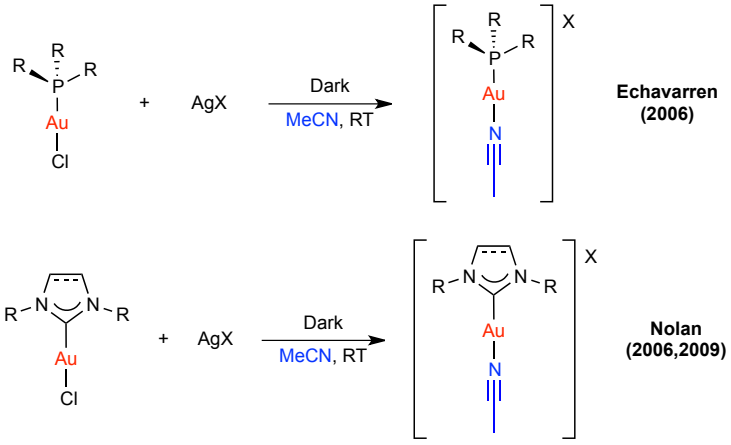
Scheme 5. Routes towards the synthesis of gold-triflimide complexes

Gold-triflimide complexes have proven to be very versatile catalysts. However, they are ineffective for some gold-catalysed transformations. A good alternative to such complexes is the use of stable gold solvate species, which offer a more flexible choice of counterion.

❖ **Stable solvate [Au(L)(MeCN)][X] species**

Cationic gold species [Au(L)]$^+$ can be stabilised by coordination of a solvent molecule. However, in order to secure the catalytic activity of the newly formed species, the solvent has

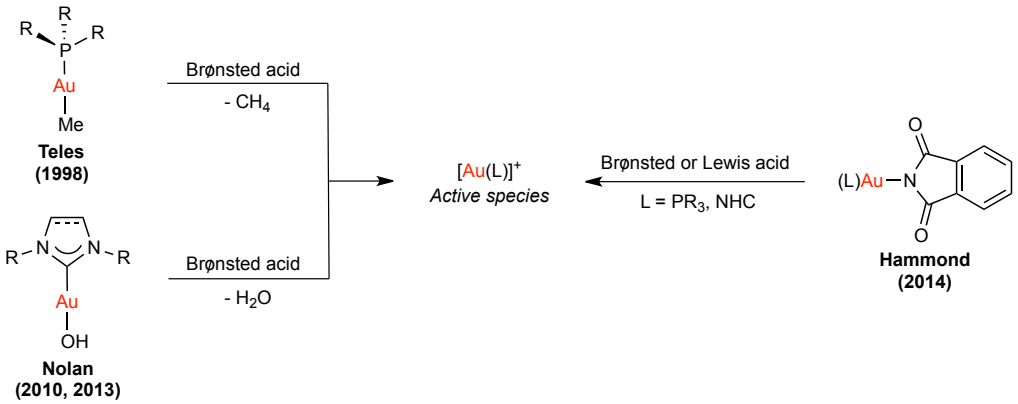
to be weakly coordinated and able to be easily replaced by unsaturated substrates. There are examples of gold solvate species with, for example toluene,[24] THF,[25] pyridine[25] and NH_3.[26] Nevertheless, the most common gold solvate complexes encountered in the literature are based on coordination to acetonitrile; [Au(L)(MeCN)][X] (L = PR_3 or NHC, X = BF_4, SbF_6, PF_6, etc.).[25,27] This species have proven to be highly stable and active in a myriad of gold-catalysed transformations and some of them, such as [Au(IPr)(MeCN)][BF_4] and [Au(JohnPhos)(MeCN)][SbF_6] are commercially available. [Au(L)(MeCN)][X] complexes can be easily synthesised by reacting [Au(L)Cl] and AgX in dry acetonitrile (Scheme 6).



Scheme 6. Most common gold solvate species

❖ Acid activation of organogold complexes

In his seminal work on the gold-catalysed hydroxalkoxylation of alkynes, Teles and co-workers used an organogold complex activated by a Brønsted acid.[28] Since then, the use of [Au(PR_3)(Me)] activated by HX (X = BF_4, OTf, RSO_3, SO_4H, etc) has been scarce. Our group has contributed to this area with a study on the acid activation of [Au(NHC)(OH)] complexes.[29] This has led to the development of new silver free protocols for gold catalysis,[30] including the synthesis and isolation of [{Au(NHC)}$_2$(μ-OH)][X] species (See Chapter 5 for more details).[29,31] In addition, Hammond and co-workers have recently reported the synthesis of [Au(L)(Pht)] (L = PR_3 or NHC, Pht = phthalimide), which is an inactive catalyst itself.[32] However, upon addition of a Brønsted or Lewis acid it delivers a highly active catalytic species (Scheme 7).



Scheme 7. Selection of acid activated organogold complexes

1.1.3 *Mono- and Di-Nuclear Gold Hydroxide Species*

Late transition metal (LTM) hydroxide species have been described as versatile and environmentally friendly reagents in organometallic synthesis and have been proposed as plausible intermediates in a myriad of catalytic transformations.[33] At the beginning most of these species were serendipitously isolated and regarded as undesired products. However, during the last two decades much effort has been dedicated to the development of reliable synthetic routes towards this species.[33] One of the reasons why LTM-OH species are fascinating is that, theoretically, they should not be stable. According to the Hard and Soft Acids and Bases theory,[34] this kind of species represent one of the biggest mismatches one can encounter. While the hydroxo ligand is a hard base (small atomic radius, high electronegativity), late transition metal ions are soft acids (big atomic radius, low oxidation states).[34] Therefore, this soft acid/hard base mismatch affords relatively weak LTM-OH bonds, which confers both advantageous and detrimental properties to transition metal hydroxide species. While a weak LTM-OH bond means that the OH moiety can be easily substituted by other ligands, thus granting access to a wide range of organometallic complexes; it also means that LTM-OH species can be highly unstable. This dichotomy has encouraged chemists to pursue the synthesis, characterisation and reactivity studies of this fascinating family of organometallic species.[33]

One of the main interests of our group is the study of transition metal hydroxide species, and as a result of our investigations several LTM-OH complexes have been reported (Figure 4): Au-OH,[23a] Cu-OH,[35] Ru-OH,[36] Pd-OH,[37] Rh-OH,[38] and Ir-OH[39] species. Everything started with the synthesis, isolation and reactivity studies of the first mononuclear gold hydroxide species.[23a]

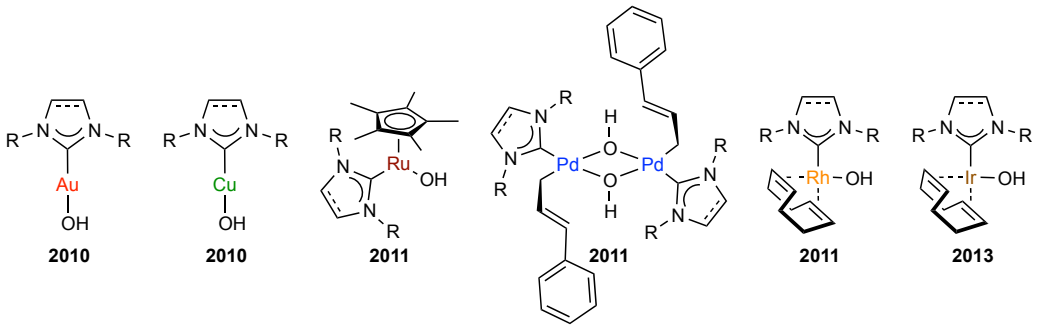


Figure 4. LTM-OH species reported by our group

1.1.3.1 [Au(IPr)(OH)]: A Golden Synthon

In 2007, our group in collaboration with Maseras and co-workers, reported the gold-catalysed formation of α,β-unsaturated ketones from propargylic acetates in aqueous media.[40] During a combined experimental and theoretical study on the reaction mechanism, it was suggested that an unprecedented [Au(NHC)(OH)] species could be the active catalyst. In addition, DFT calculations predicted this complex to be highly stable, and thus isolable (Figure 5). Due to the unique nature of such species in gold chemistry, our group became highly interested in trying to synthesise and isolate a Au-OH complex.

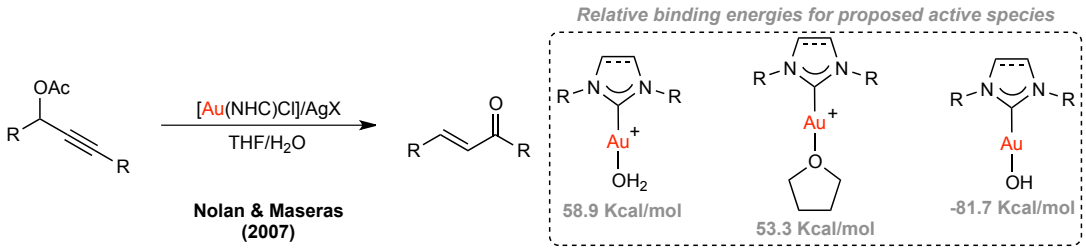
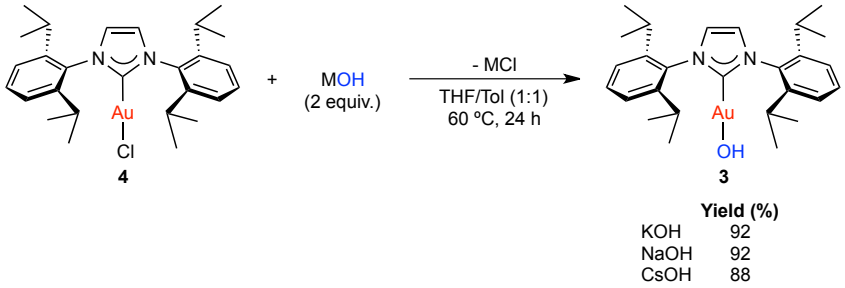


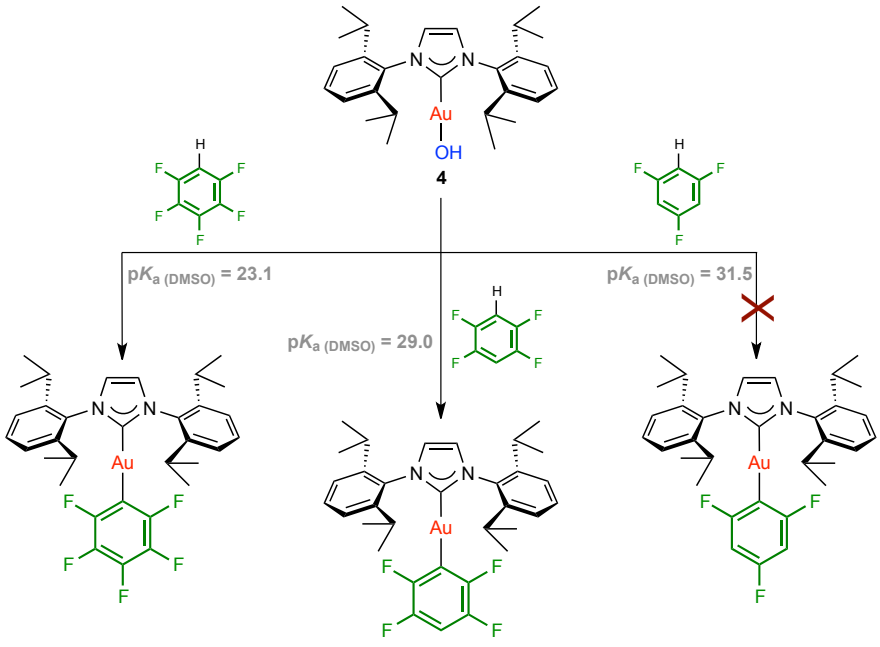
Figure 5. Synthesis of α,β-unsaturated ketones from propargylic acetates and predicted active species

Gratifyingly, in 2010 we reported the isolation of the first monomeric, dico-ordinated, gold(I) hydroxide species bearing a NHC as an ancillary ligand.[23a] The synthesis of such a complex was accomplished by reacting [Au(IPr)Cl] (**3**) with an excess of a suitable hydroxide source (either CsOH, NaOH or KOH) in a mixture of THF/toluene, at 60 ºC for 24 h. All the alkali salts afforded the desired gold hydroxide [Au(IPr)(OH)] (**4**) in high yields, 88-92% (Scheme 8). Noteworthily, this procedure proved to be quite robust and the reaction proceeded under air and using technical grade solvents. However, during the characterisation process it was noted that traces of acid in chlorinated solvents, such as CD_2Cl_2 or $CDCl_3$, led to partial regeneration of **3**. Therefore, it was necessary to filter such solvents through basic aluminium oxide in order to remove traces of HCl.



Scheme 8. Synthesis of **4** by salt metathesis of **3** and MOH (M = K, Na, Cs)

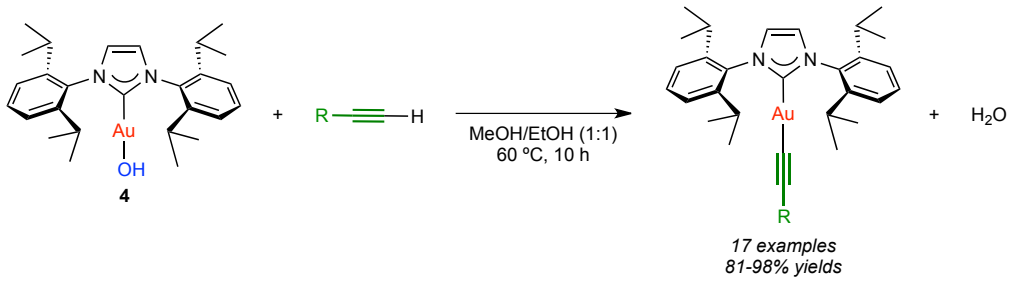
Once hydroxide **4** was isolated it was tested in the formation of α,β-unsaturated ketones, where it had been predicted to be the active species. Disappointingly, **4** proved to be completely inactive for this transformation.[29] However, further investigations on the reactivity of **4** showed that it could be a versatile reagent for the activation of Y-H (Y = O, N, C) bonds.[23a] Preliminary studies on the reactivity of **4** with several fluoroarenes allowed our group to determine that hydroxide **4** can activate Y-H bond with a $pK_{a\,(DMSO)}$ < $pK_{a\,(DMSO)}$ of water (31.4) (Scheme 9). Thus, **4** can react with pentafluorobenzene ($pK_{a\,(DMSO)}$ = 23.1) and 1,2,4,5-tetrafluorobenzene ($pK_{a\,(DMSO)}$ = 29.0), but not with 1,3,5-trifluorobenzene ($pK_{a\,(DMSO)}$ = 31.5) (Scheme 8).[23a,41] Later, the exact $pK_{a\,(DMSO)}$ of hydroxide **4** was calculated by potentiometric titrimetry to be 30.3(2).[42]



Scheme 9. Activation of fluoroarenes by hydroxide **4**

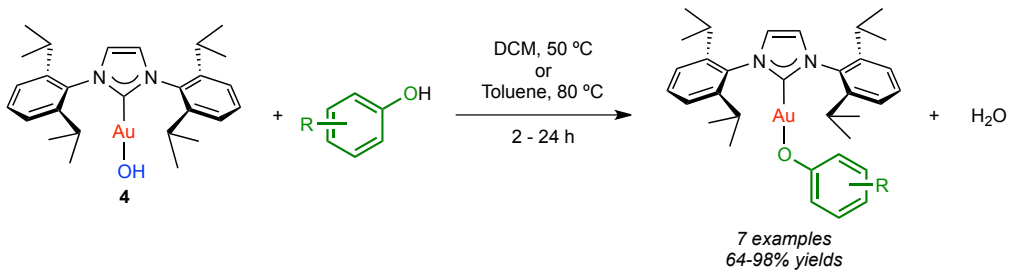
Taking advantage of the Brønsted basic character of **4**, several straightforward protocols for the synthesis of organogold complexes were devised. It is worth noting that the only by-product generated during these reactions is water, thus making these approaches quite

environmentally friendly. For example, upon reaction of hydroxide **4** with terminal alkynes several gold-acetylide species were synthesised in excellent yields (81-98%) (Scheme 10).[43] Interestingly, several of these gold-acetylide species were found to be luminescent, emitting in wavelengths corresponding to blue-green and blue in the visible spectra.[43] Moreover, for some complexes their quantum yields were determined to be higher than their phosphane analogues.[43]



Scheme 10. Synthesis of gold-acetylide species using **4**

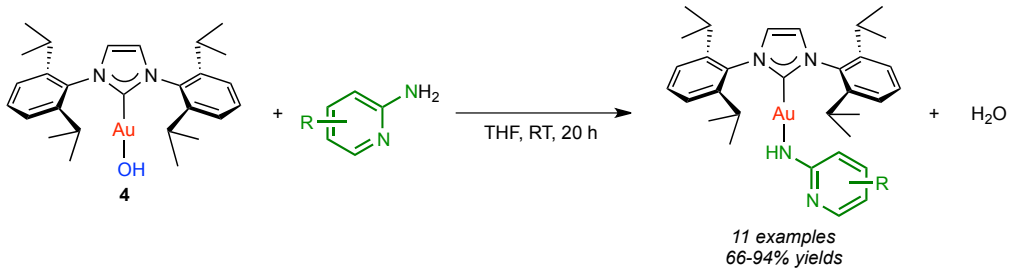
In addition, hydroxide **4** has also been used to prepare gold-phenolate complexes.[44] Reaction of **4** with several phenol derivatives led to the isolation of a number of gold-phenolate species in good to excellent yields (68-99%) (Scheme 11).[44] Interestingly, these species can also be synthesised *via* a mechanochemical approach. Grinding [Au(IPr)Cl] with a phenol in the presence of KOH allowed the isolation of several gold-phenolate derivatives in short reaction times and provides a more environmentally friendly protocol, as it eliminates the need for auxiliary solvents.[44] An independent study carried out by Hashmi and co-workers showed that these gold-phenolate derivatives are catalytically active in the hydration of terminal alkynes;[45] although significantly less active than the most common gold catalysts.



Scheme 11. Synthesis of gold-phenolate species using **4**

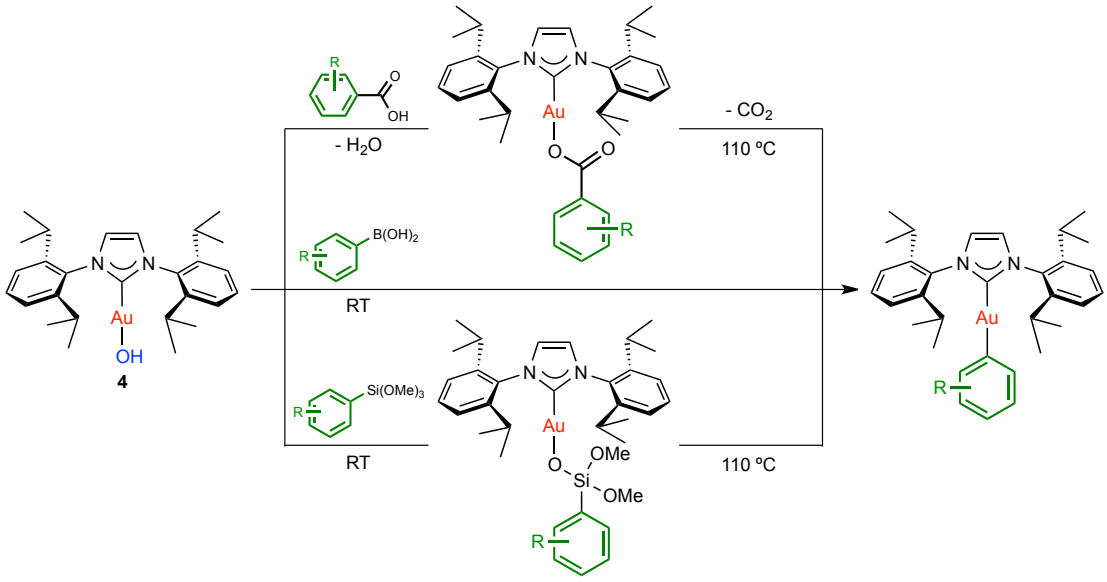
Toste and Bergman have recently reported the synthesis of a series of gold-amide species upon reaction of [Au(NHC)Cl] with lithium amide reagents.[46] Alternatively, we have reported a more environmentally friendly protocol using hydroxide **4** to activate several N-H bonds (Scheme 12). Reaction of **4** with several anilines allowed the isolation of gold-anilide species

in good to excellent yields, producing water as the sole by-product. Moreover, some of these gold-anilide complexes showed interesting luminescent properties.[47]



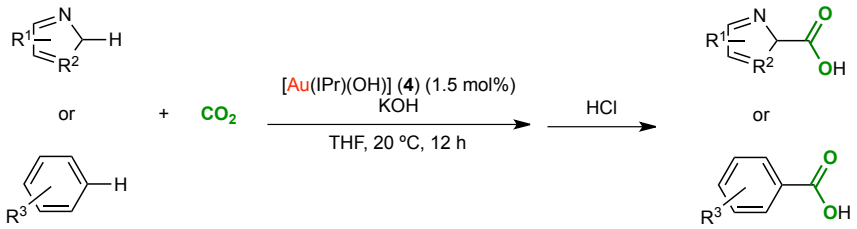
Scheme 12. Synthesis of gold-anilide species using **4**

Hydroxide **4** has also proven to be able to react with aryl-carboxylic acids, forming the corresponding gold-carboxylate species, that upon heating would release CO_2 thus forming gold-aryl complexes in an easy and straightforward manner.[48] Alternatively, these kind of species could also be synthesised by reacting **4** with aryl-boronic acids[49] or with siloxanes, which are generally cheaper (Scheme 13).[50] Interestingly, if the latter reaction is performed at room temperature it leads to the formation of a gold-siloxane intermediate that upon heating would deliver the desired gold-aryl species.[50]



Scheme 13. Synthesis of [Au(IPr)(aryl)] species using **4.**

These gold-aryl species have been proposed as viable reaction intermediates in a myriad of gold-catalysed processes. For example, our group has successfully reported the carboxylation of several (hetero)aromatic compounds upon reaction of hydroxide **4** with suitable organic substrates ($pK_{a\,(DMSO)} < 30.2(2)$) under CO_2 atmosphere (Scheme 14).[42]



Scheme 14. Carboxylation of C-H bonds catalysed by **4**

Although hydroxide **4** has shown little catalytic activity itself,[29] it has proven to be a very good source of $[Au(IPr)]^+$, the proposed active species in gold catalysis, upon acid activation; thus opening the door to the development of new silver free protocols for gold catalysis (see section 1.1.2.2. for more information).[29-30,51] Interestingly, during the studies on the acid activation of **4**, a new gold complex was isolated: $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ (**5**).[29]

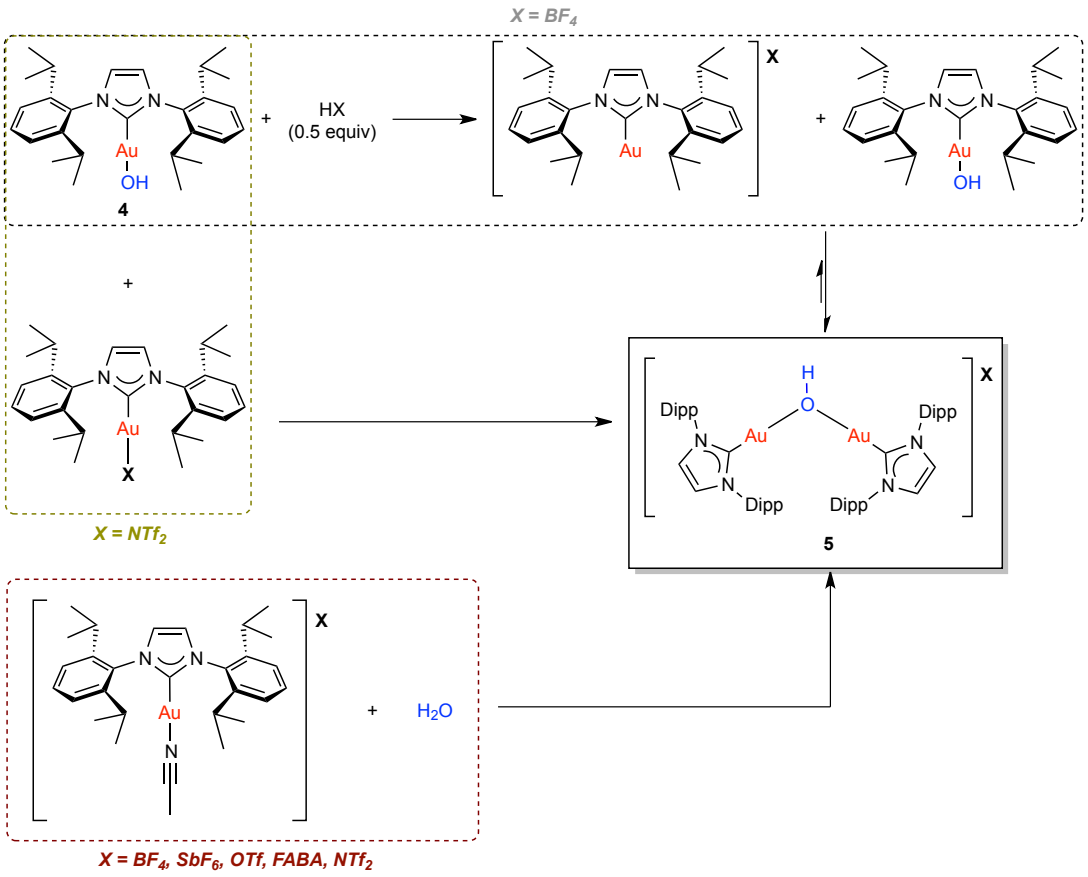
1.1.3.2 Digold Hydroxides

Initial reaction of [Au(IPr)(OH)] (**4**) with 1 equiv. of a Brønsted acid, $HBF_4 \bullet OEt_2$, revealed the formation of a new gold species by ^1H NMR spectroscopy, $[Au(IPr)(OEt_2)][BF_4]$, which was in equilibrium with $[Au(IPr)][BF_4]$ (eq. 2).[29]

$$[Au(IPr)(OH)] + HBF_4 \cdot OEt_2 \xrightarrow[-\ H_2O]{} [Au(IPr)][BF_4] \rightleftharpoons [Au(IPr)(OEt_2)][BF_4] \qquad (2)$$

Both species proved to be stable in solution for several days, but unfortunately they could not be isolated. As $HBF_4 \bullet OEt_2$ is a fuming acid, the possibly of replacing it with an aqueous HBF_4 solution was then investigated. Surprisingly, reaction of hydroxide **4** with the latter resulted in formation of $[Au(IPr)][BF_4]$ which would with time evolve to a new complex. It was hypothesised that water could promote the formation of this new complex.[29] Therefore, the reaction was repeated in the presence of water, which gratifyingly promoted the formation of the new species. Crystals suitable for single crystal X-ray diffraction analysis were grown revealing this new species as $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ (**5**).[29] A closer look at the structure revealed that the Au-$C_{carbene}$ distances in **5** were in between those found in neutral species such as **4** and cationic gold complexes such as for example $[Au(IPr)(MeCN)][BF_4]$. Suggesting that **5** could be viewed as a combination of neutral and cationic gold centres. This hypothesis was later supported by reaction of hydroxide **4** with half an equivalent of an aqueous HBF_4 solution, resulting in quantitative formation of digold species **5**.[29] In addition, if **4** is reacted with 1 equivalent of $[Au(IPr)NTf_2]$, digold hydroxide **5** is also obtained in quantitative yields.[31a] Later it was discovered the digold hydroxide **5** could also be synthesised starting from a cationic gold species, such as $[Au(IPr)(MeCN)][BF_4]$, by simply

dissolving it in an organic solvent in the presence of water.[31a] A summary of the synthetic routes towards **5** can be found in Scheme 15.



Scheme 15. Synthetic routes towards digold hydroxide complexes

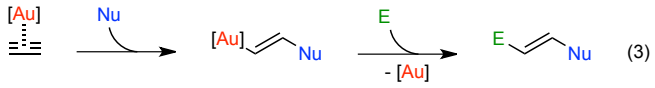
Since digold hydroxide **5** was easily formed from cationic gold complexes in aqueous media, it was proposed as a possible active species in water-inclusive gold-catalysed transformations. Indeed, **5** performed very well without the need of external additives, in alkyne and nitrile hydration, as well as Meyer-Schuster rearrangement and the formation of α,β-unsaturated ketones from propargylic acetates.[29,31a]

Further studies on catalytic applications of digold hydroxides as silver free catalysts, as well as dual activation catalysts, can be found in Chapters 5 and 7, respectively. Moreover, details on the use of **5** for the synthesis of interesting gold species such as *gem*-diaurated and σ,π-digold-acetylide complexes can be found in Chapter 6. Next, we present a brief discussion about the importance that the latter species are gaining in gold catalysis.

1.1.4 *Renaissance of Diaurated Species as Important Catalytic Intermediates*

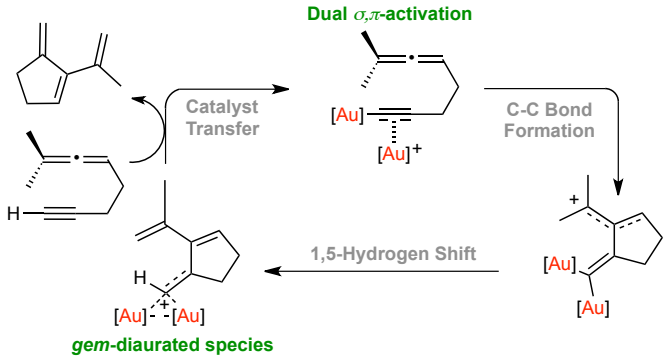
As explained in section 1.1.1, Au^{I} complexes display unique properties that make them ideal catalyst to activate C-C multiple bonds towards nucleophilic attacks. It was assumed

from an early stage that gold-catalysed reactions proceeded through the interaction of *one* gold centre with *one* substrate molecule. A simplified gold catalysed process can be explained in 3 steps: a) π-coordination of the catalyst to the alkyne/allene/olefin; b) nucleophilic attack from the substrate; and c) deauration of the intermediate through reaction with an electrophile (eq. 3).



(3)

However, the seminal work published by Toste in 2008,[52] opened the door to question this assumption. There he proposed that not one, but *two* gold centres could interact with *one* substrate molecule, therefore generating two new kind of complexes: a) σ,π-digold acetylide and b) *gem*-diaurated species. In the reported computational studies, which were supported by experimental data, it was found that the most plausible reaction mechanism involved a dual *σ,π*-type activation of the terminal alkyne by two molecules of $[Au]^+$. This reaction sequence was followed by cycloisomerisation, generating a *gem*-diaurated species that reacted with a new substrate molecule to release the final product (Scheme 16).



Scheme 16. Mechanistic proposal involving *gem*-diaurated and σ,π-digold-acetylide species

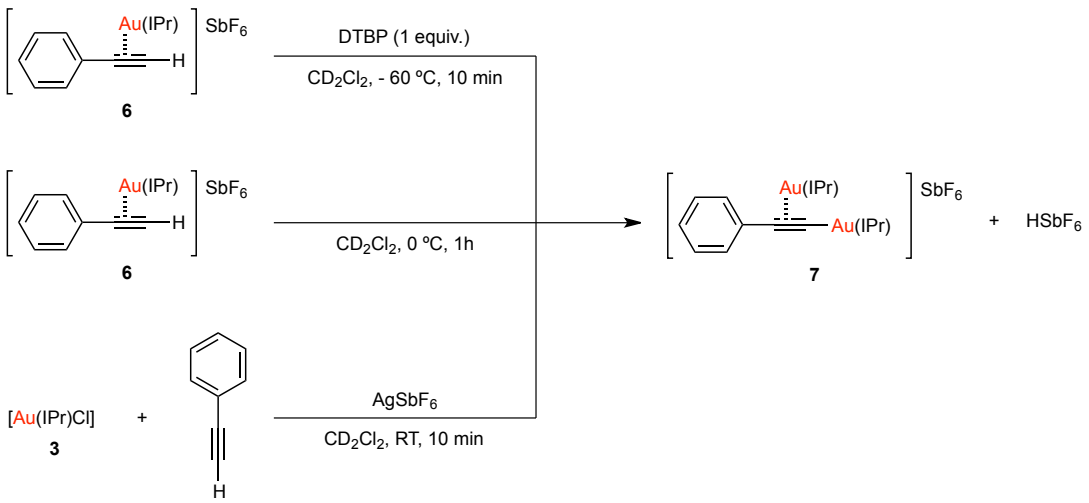
This work raised questions about the interactions between Au^I-complexes and terminal alkynes and the mechanism by which gold catalyses organic transformations. Since then, several research groups have enormously contributed to our understanding of both σ,π-digold acetylides and *gem*-diaurated complexes and their role in catalysis. Moreover, these studies have led to the development of a novel type of gold-catalysed transformations that require dual activation of the substrate by the gold catalyst.[53]

1.1.4.1 σ,π-Digold Acetylides

After Toste's initial report, Widenhoefer[54] and Corma,[55] independently began to explore the dual activation of alkynes by Au^I-complexes shedding light on how this dinuclear gold

species can be easily generated *in situ* from mononuclear gold complexes reacting with a terminal alkynes. While Widenhoefer focused on the synthesis and stability of σ,π-digold-acetylide complexes,[54] Corma investigated their importance as intermediates in catalytic transformations.[55]

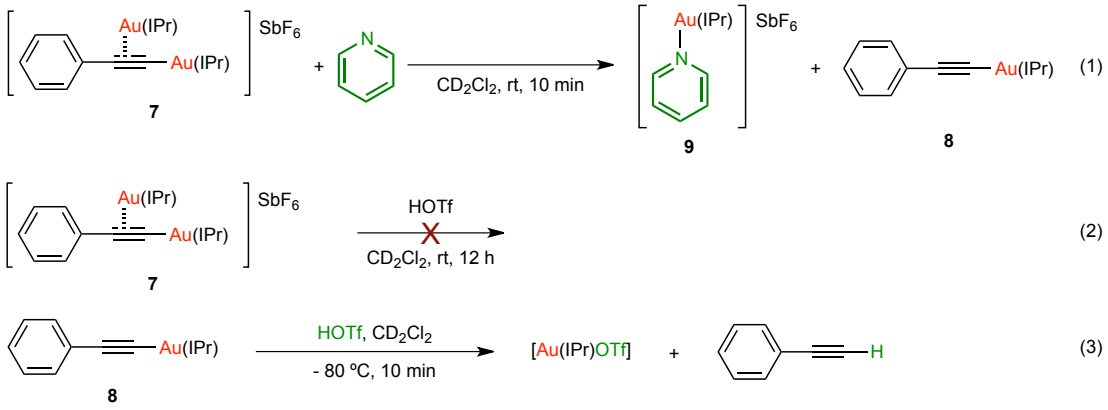
Widenhoefer began his studies by reacting well-defined cationic π-acetylide species, such as [Au(IPr)(η^2-HC≡CPh)][SbF_6] (**6**), with 1 equiv. of base at low temperatures. This reaction afforded the dinuclear gold species [{Au(IPr)}$_2$(η^1, η^2-C≡CPh)][SbF_6] (**7**) in short reaction times. In addition, if **6** was kept in a CD_2Cl_2 solution at 0 ºC, it formed diaurated species **7** within 1 h. Further investigations revealed that **7** could be easily synthesised in very good yields by reacting a mixture of [Au(IPr)Cl] (**3**) and $AgSbF_6$ with an excess of phenylacetylene at 25 ºC for 10 min (Scheme 17).[54] Formation of diaurated species **7** also generates 1 equiv. of a strong Brønsted acid ($HSbF_6$). Since σ,π-acetylide **7** was easily generated in the absence of a base, it was suggested that this type of species may be involved in gold-catalysed transformations engaging terminal alkynes.[54]



Scheme 17. Routes towards formation of diaurated speceis **7** described by Widenhoefer

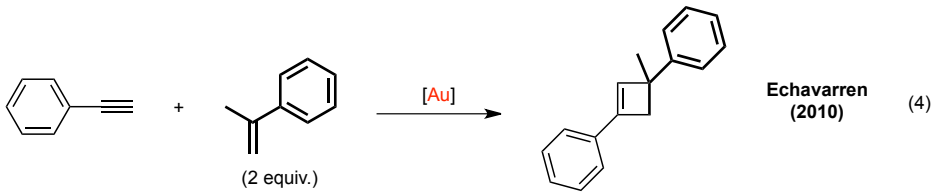
The stability of the σ- and π-bonds was subsequently investigated (Scheme 18). Addition of a two-electron donor ligand, such as pyridine, to a solution of **7** led to a 1:1 mixture of the neutral σ-acetylide species [Au(IPr)(C≡CPh)] (**8**) and the cationic complex [Au(IPr)(Py)][SbF_6] (**9**) after 10 min at 25 ºC (eq. 1, Scheme 18). Furthermore, evaluation of the stability of **7** towards protodeauration revealed that σ,π–acetylide species were much more stable towards this process than their mononuclear congeners. Addition of HOTf to a solution of **7** did not afford any product after 12 h at 25 ºC (eq. 2, Scheme 18), while reaction with acetylide **8** led to complete conversion into [Au(IPr)(OTf)] after 10 min at -80 ºC (eq. 3,

Scheme 18). Finally, Widenhoefer and co-workers proposed that as formation of diaurated species **7** generates 1 equiv. of a strong Brønsted acid ($HSbF_6$), the latter could have an influence on reactions where such species are formed.

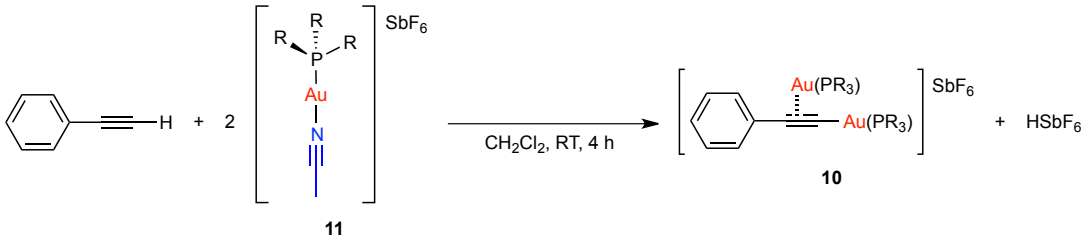


Scheme 18. Stability of **7** towards a two-electron donor and acid species

This hypothesis was independently confirmed by Corma[55] while studying the mechanism of the intermolecular [2+2] cycloaddition of alkynes with alkenes reported by Echavarren (eq. 4).[56]



During the course of his investigations, Corma observed the formation of a digold species of the type $[\{Au(PR_3)\}_2(\eta^1, \eta^2\text{-}C{\equiv}CPh)][SbF_6]$ (**10**), resulting from the reaction involving a cationic gold complex $[Au(L)(MeCN)][SbF_6]$ (**11**) and phenylacetylene (Scheme 19).[55]

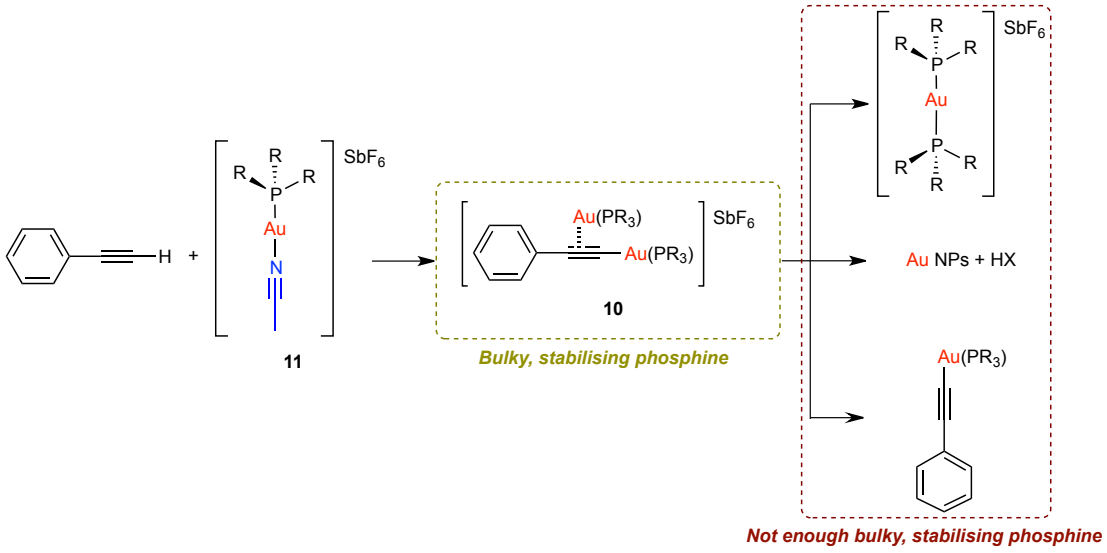


Scheme 19. Synthesis of **10** reported by Corma

The use of **10** as catalysts enhanced the selectivity of the reaction towards the alkene, allowing the use of 1:1 alkyne:alkene *vs.* the 1:2 ratio described by Echavarren, although at the cost of lower activity than **11**.[55] Corma also studied how the Brønsted acid generated *in*

situ during the formation of **10** could influence the reaction. Such acid could either react with the alkene, promoting polymerization of the substrate, or with the final product, thus reducing the selectivity and yields of the process. Although Corma demonstrated that diaurated σ,π–acetylide species could be active intermediates in catalysis, it is worth mentioning a recent contribution by Gimbert where a combination of computational and experimental studies has shown the lack of reactivity of such species in the cycloisomerisation of 1,6-enynes.[57]

A more recent communication by Corma has shed more light on the reactivity of these σ,π–acetylide species.[58] Using a combination of NMR and mass spectroscopic techniques, Corma was able to study the tendency of gold-phosphine complexes to form diaurated species under the conditions in which gold catalysis is carried out. His study concluded that while $[Au(PR_3)]^+$ have a high tendency to form diaurated species when dealing with terminal alkynes, the stability of this digold σ,π-acetylide species is determined by the steric hindrance of the ligand: bulky phosphines stabilise them while less sterically demanding ligands lead to decomposition of the digold-acetylide into monogold complexes and gold nanoparticles (Scheme 20).[58]



Scheme 20. Stability of diaurated species depending on the steric hindrance of the ligand

1.1.4.2 Gem-diaurated Species

Geminally diaurated complexes have been known since the mid 1970s.[59] However, they were considered as mere curiosities. It was not until Gagné and co-workers reported the isolation and characterisation of a *gem*-diaurated species, more than 30 years after the original report, that these begun to attract the attention of the scientific community (Figure 6).[60]

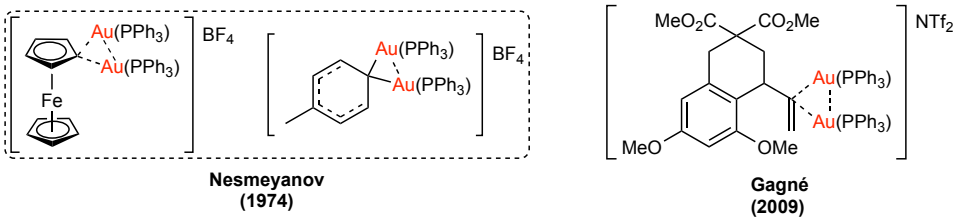


Figure 6. *Gem*-diaurated species reported by Nesmeyanov and Gagné

Since then, several reports have focused on the formation and characterisation of *gem*-diaurated complexes, highlighting their significance as a possible catalyst resting state in some Au^{I}-catalysed transformations. Several research groups have most notably contributed to our understanding of the chemistry of those species.[2g,60-61] Among these, three contributions deserve special mention: Fürstner, Gagné and Gray.

Fürstner and co-workers followed Gagné's initial report with a systematic investigation on the significance of *gem*-diaurated intermediates in catalytic reactions.[61b] As a result of their studies the following insights on the nature and reactivity of these type of species was gained: a) the nature of the bond between the two gold centres and the olefin can be as a three-centre two-electron system or as two regular σ Au-C bonds flanked by a stabilised cationic centre; b) *gem*-diaurated species are quite resistant to protodeauration processes, thus this key step must proceed through a vinyl intermediate (Figure 7).

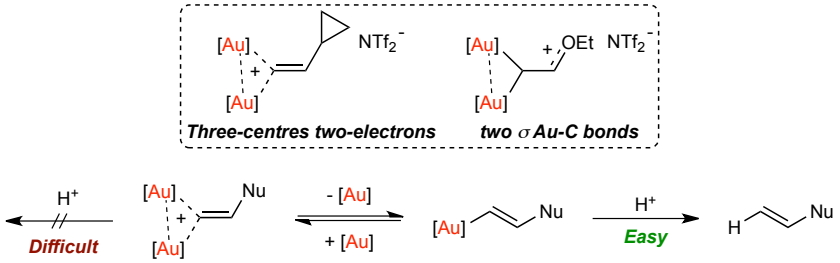


Figure 7. Conclusions from Fürstner's studies on *gem*-diaurated species

Gagné and co-workers have recently reported on the strong electronic and counterion effects on the formation and reactivity of *gem*-diaurated species.[61a] In their studies, a series of Au^{I}-aryl complexes were used as models for catalytic vinyl gold intermediates, instead of the corresponding *gem*-diaurated vinyl species due to the low stability of the latter. Three main conclusions can be drawn from their work: a) the electron-density of the aryl and vinyl ligands has a high impact on the reactivity of the digold species, the most reactive being those bearing less electron-rich ligands; b) the tendency to form *gem*-diaurated species is higher for counterions with poorer coordinating ability, and c) the presence of gold salts can affect the rate of protodemetalation of mononuclear Au^{I}-aryl/vinyl species as they can, depending on the nature of the counterion, promote the generation of digold species and thus inhibit this

process.[61a] These statements should be taken into account when considering the use of certain catalysts for multi-step reactions as less coordinating counterions are typically chosen to accelerate the initiation step, but at the same time these promote the formation of digold intermediate species that are more stable, and thus less reactive.[61a]

In addition, Gagné has also recently observed a new coordination mode for diaurated species. Through a combination of NMR studies and single crystal diffraction analysis, they were able to distinguish for the first time between a *gem*-diaurated species and a complex with a σ,π-binding mode between the two gold centres and the olefin (Figure 8).[62] This was achieved by using bulky phosphine ligands to increase the steric hindrance around the gold centres.[62]

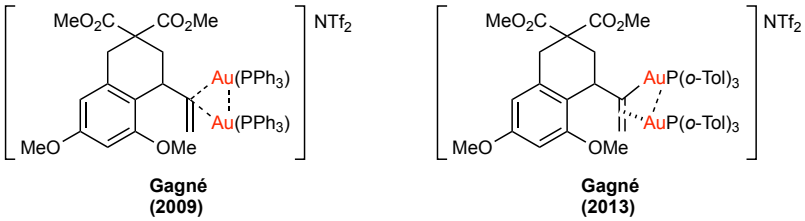
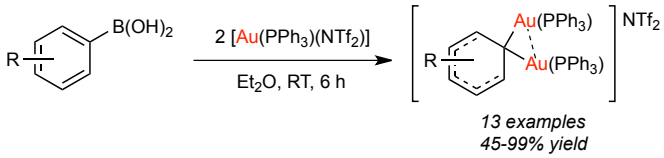


Figure 8. Different coordination in diaurated species depending on the steric hindrance

Although Fürstner and Gagné enormously contributed to our understanding about *gem*-diaurated species, there was still a lack of easy and robust methodologies for their synthesis. These species were usually synthesised in *via* a two-step protocol, where a monoaurated complex was first isolated and then 1 equiv. of a cationic gold species was added to yield the desired *gem*-diaurated compound. Therefore, the development of a more straightforward route was highly desirable. This issue was solved by Gray and co-workers, who have recently reported the first straightforward methodology to obtain aromatic *gem*-diaurated species in high yields under mild conditions.[63] By reacting 2 equiv. of $[Au(PPh_3)(NTf_2)]$[22b] with 1 equiv. of an aryl boronic acid in diethyl ether at 25 ºC, they were able to isolate several $[\{Au(PPh_3)\}_2(\mu\text{-aryl})][NTf_2]$ complexes (Scheme 21).[63]

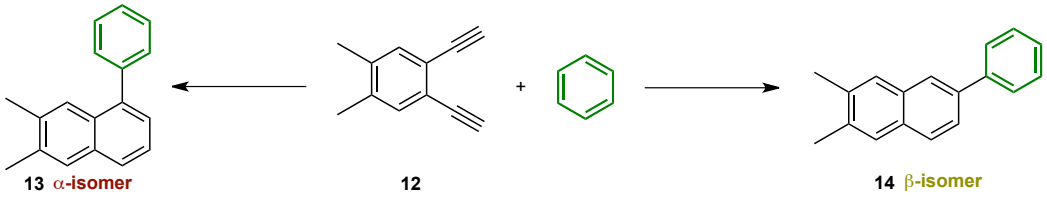


Scheme 21. First straightforward methodology for the synthesis of *gem*-diaurated species

1.1.4.3 Significance of σ,π-Digold-Acetylides and gem-Diaurated Species in Catalysis

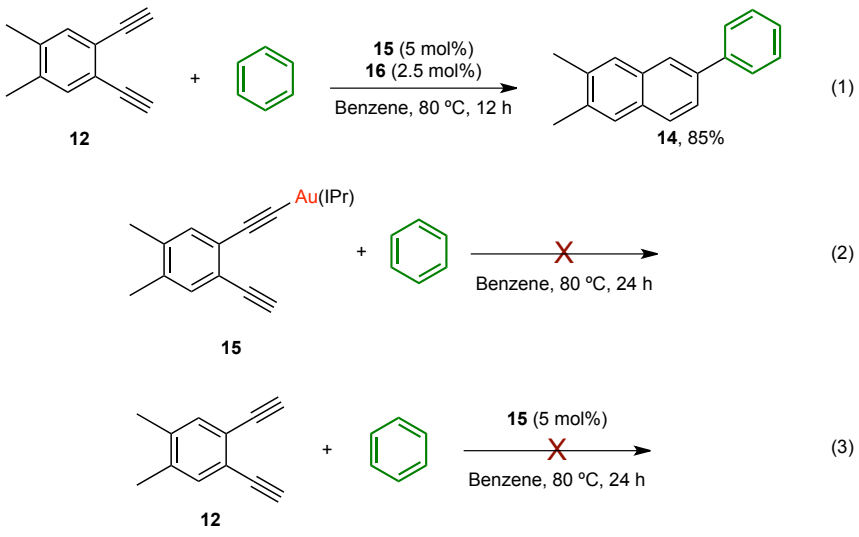
Following the work of Toste,[52] Hashmi has recently extensively reported on the dual activation of diynes leading to *gem*-diaurated intermediates.[53,64] As an example of how the involvement of such species can affect the reactivity in gold catalysis a detail discussion about Hashmi's firsts reports is presented next.

In their early contribution, mechanistic investigations on the α/β-selectivity of a cycloaddition between diyne **12** and benzene reaction were performed.[64b,64d] They showed that several factors could affect the selectivity: the α-isomer (**13**) was the major product at high catalyst loadings and low temperatures, and the formation of the β-isomer (**14**) was preferred in the presence of basic additives (Scheme 22).



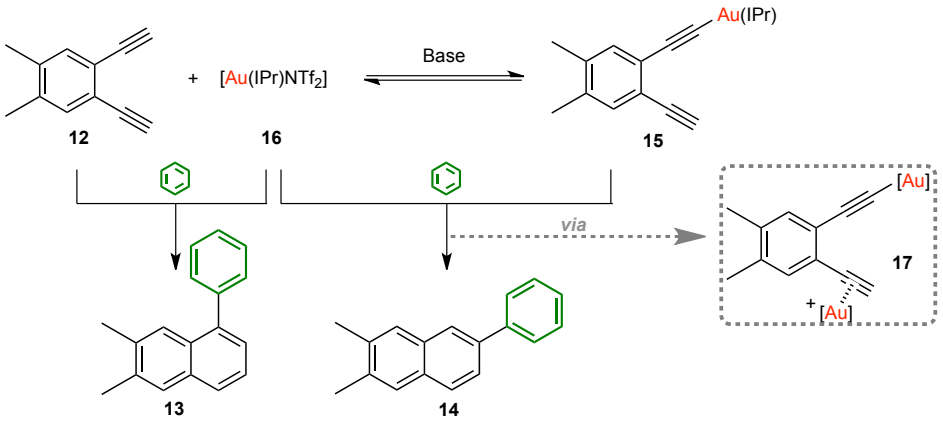
Scheme 22. Switch in selectivity between α– and β-isomers

The latter result suggested the possible formation of the Au-acetylide species **15** during the β-catalytic cycle. To support this, several reactions of **15** and diyne **12** were performed. Surprisingly, mixing catalytic amounts of acetylide **15** and Gagosz's catalyst [Au(IPr)(NTf$_2$)][22a] (**16**) led to almost complete conversion of diyne **13** into the β-isomer (eq. 1, Scheme 23), while the use of either catalytic or stoichiometric amounts of **15** led to no reaction (eq. 2-3, Scheme 23).



Scheme 23. Stoichiometric and catalytic reactions involving **15**

This suggested that an equilibrium exists between **12**, **15** and **16**.[64d] If the gold complex **16** reacts with diyne **12** in the absence of additives, the α-product is the major one, while if formation of acetylide **15** is favoured, e.g. by the addition of a base that would further react with diyne **12** to form the dual activated intermediate **17**, then the β-isomer is formed (Scheme 24).



Scheme 24. Proposed equilibrium between **12**, **15** and **16**, and consequences in selectivity.

Attempts to gain insights into the reaction mechanism afforded the isolation of Au^{I}-aryl (**18**) and *gem*-diaurated (**19**) species (Figure 9).

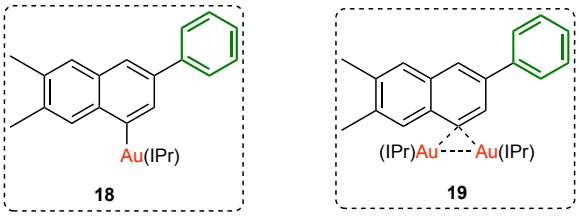
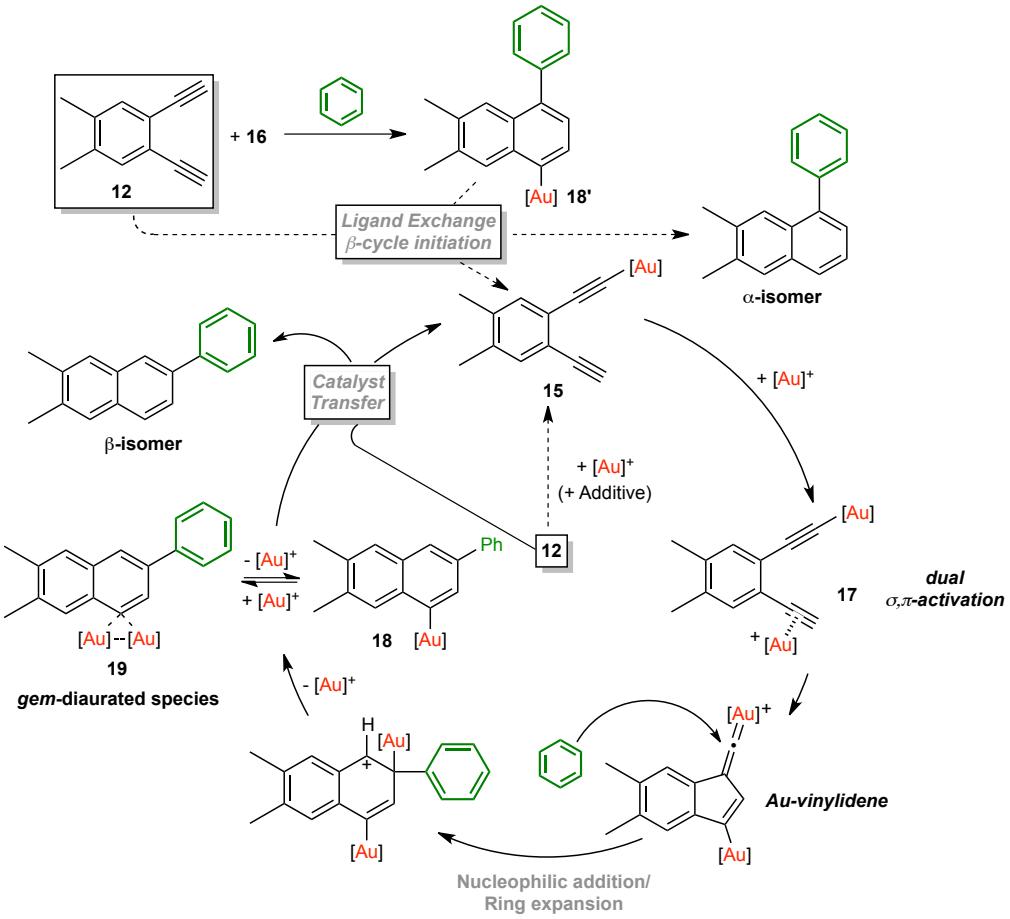


Figure 9. Isolation of possible reaction intermediates **18** and **19**

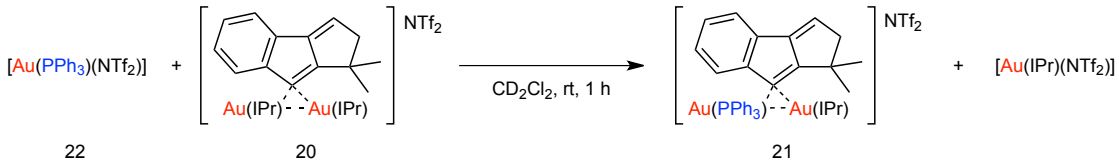
The catalytic reaction using 5 mol% of aryl-gold complex **18** afforded only 5 mol% of β-isomer, due to protodemetalation by diyne **12** and formation of gold acetylide **15**. However, addition of gold complex **16** afforded the desired β-isomer **14** in high yields. Gratifyingly, the use of 2.5 mol% of *gem*-diaurated complex **19** afforded the β-isomer in high yields even in the absence of additional catalyst. Further investigations revealed that diaurated species **19** was involved in an equilibrium with aryl-gold complex **18** and free catalyst **16** at high temperatures and is the reason the reaction proceeds.[64d] This makes *gem*-diaurated species **19** an excellent "*off-cycle*" or "*reservoir*" catalyst for this transformation. This concept was also later proposed by Widenhoefer and Gagné for the gold-catalysed intramolecular hydroxalkoxylation of allenes.[65]

The catalytic cycle proposed for the β-selectivity is as follows: initial reaction of Gagosz complex **16** with diyne **12**, followed by subsequent addition of benzene to afford arylgold species **18'**; then protodeauration by another diyne molecule forms acetylide **15** and starts the β-catalytic cycle (Scheme 25).[64d]



Scheme 25. Catalytic cycle proposed by Hashmi

This catalytic cycle could be considered as a general scheme for the reactions involving diyne-type substrates described by Hashmi.[53] The recent follow-up communication deals with the role of this *gem*-diaurated species in the synthesis of benzofulvenes and sheds further light on the role of digold species in catalysis.[64e] Hashmi has developed an alternative synthetic protocol to the one of Zhang,[66] identifying and isolating the *gem*-digold species **20** as an excellent rapidly activated pre-catalyst for this reaction type.[64e] By using **20** as catalyst, the reaction time could be reduced 3-fold.[64e] In the course of their studies, the first example of a *gem*-diaurated species bearing two different gold centres (**21**) was also isolated. This mixed diaurated species was formed by reacting **20** with 1 equiv. of the Gagosz triphenylphosphane complex **22** (Scheme 26).[22b] Unfortunately, no studies on how the presence of two different gold centres might affect reactivity have yet been performed.



Scheme 26. Synthesis of the first mixed-NHC/PR_3 gem-diaurated species **22**

As a result of all these investigations, researchers have developed new catalysts for gold-catalysed reactions that require a double activation of the substrate by *two* gold centres. Our group has contributed to this field with the synthesis, characterisation and reactivity studies of digold-hydroxide species (Figure 10).[29,31a] For a more detailed explanation see Chapter 7. Moreover, Hashmi has recently reported the synthesis and applications of a diaurated σ,π-acetylide complex in a wide range of transformations requiring the interaction of *two* gold centres with *one* substrate molecule (Figure 10).[64c]

Figure 10. Suitable catalyst for dual activation reactions

As scientist realised the significance of diaurated species in gold catalysis, the number of reports dealing with their characterisation and reactivity are increasing every year. However, this is a field that is still at an early stage of development and more work is needed in order to comprehend the full potential of diaurated species as reaction intermediates.

Research in the Nolan group is mainly based on the stabilisation of organometallic species bearing *N*-heterocyclic carbene (NHC) ligands. As they constitute a fundamental aspect of our research, a brief overview on the chemistry of this fascinating family of ligands is presented next.

1.2 *N*-Heterocyclic Carbenes

The term *N*-heterocyclic carbene (NHC) encloses a wide range of species, such as, for example, imidazolylidenes, imidazolidinylidenes, thiazolylidenes, oxazolylidenes, oxadiazolylidenes and triazolylidenes (Figure 11).[67] In addition, although the most common architecture is a 5-membered ring, so-called "ring expanded" analogues have also been reported. Imidazolylidene and imidazolidinylidene are the most common NHC motifs, therefore these will be the focus of the following discussion.

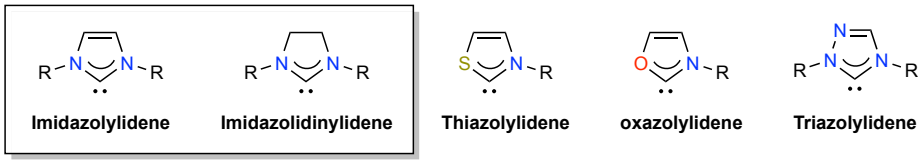


Figure 11. Selected examples of NHCs

Carbenes are divalent carbon atoms with six valence electrons. They can adopt two types of geometries at the carbon atom: a) linear or b) bent (Figure 12).[67] The linear geometry is scarce and it is based on a *sp*-hybridisation of two energetically degenerate *p* orbitals (p_x and p_y). The majority of carbenes present a bent geometry consequence of a sp^2-hybridisation. The energy of the *p* orbitals, so-called p_π, does not vary with the transition from the *sp* to the sp^2 hybridised state. Since the new sp^2 orbital, which is described as a σ orbital, presents partial *s* character it is energetically stabilised compared to the original *p* orbital.[67] In addition, depending on how electrons are distributed among the orbitals, it is possible to have either singlet or triplet carbenes at the ground state. While in the former the two non-bonding electrons can occupy the two empty orbitals ($\sigma^1 p_\pi^1$); for the latter the two electrons occupy the σ orbital with an anti-parallel spin orientation ($\sigma^2 p_\pi^0$) (Figure 12).[67]

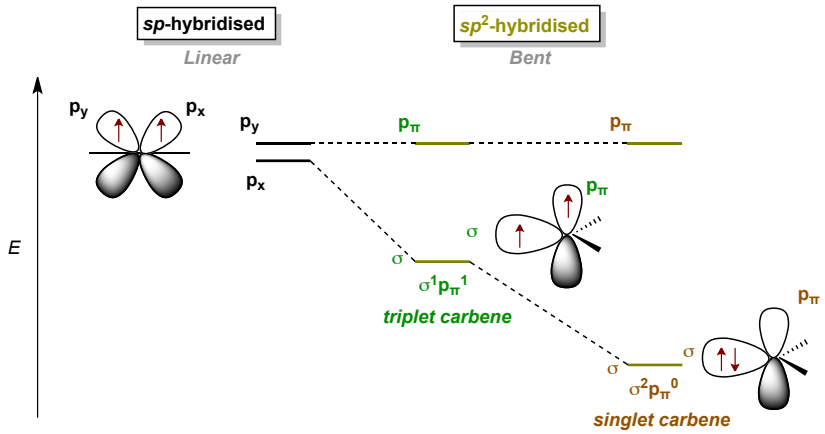


Figure 12. Most common types of carbenes

The multiplicity at the ground state is determined by the energy difference between the p_π and σ orbitals. If the energy gap between these two orbitals is relatively small, then a triplet ground state is observed; while if the energy gap is too big, a singlet ground state is observed.[67]

It has been suggested that the multiplicity can be controlled by the substituents at the carbene carbon. For example, if more electronegative substituents are used, this produces a negative inductive effect that lowers the energy of the σ orbital, while the p_π remains virtually untouched, thus stabilising the singlet state. On the other hand, if electron-donating

substituents are used, this would reduce the energy gap between σ and p_π orbitals, thus stabilising the triplet state. Moreover, the singlet state can be further stabilised if two π-donor substituents are placed next to the C atom of the carbene. The energy of the p_π orbital will rise by interaction with the π-electrons on the substituents, while the σ orbital will remain the same, thus the energy gap will increase and the singlet state will be further stabilised. The interaction between the p_π orbital and the π-electrons of the substituents will form a 4-electron-3-center π-system, which explains the partial multiple bond character observed between the π-donor atoms and the carbene carbon.[67]

This explains the high stability of NHCs at the singlet state, as the adjacent N atoms combine both σ-electron withdrawing and π-electron donating properties (Figure 13). In addition, bulky substituents at the N atom help to stabilise NHCs by sterically disfavouring the formation of the corresponding olefin dimer.[67]

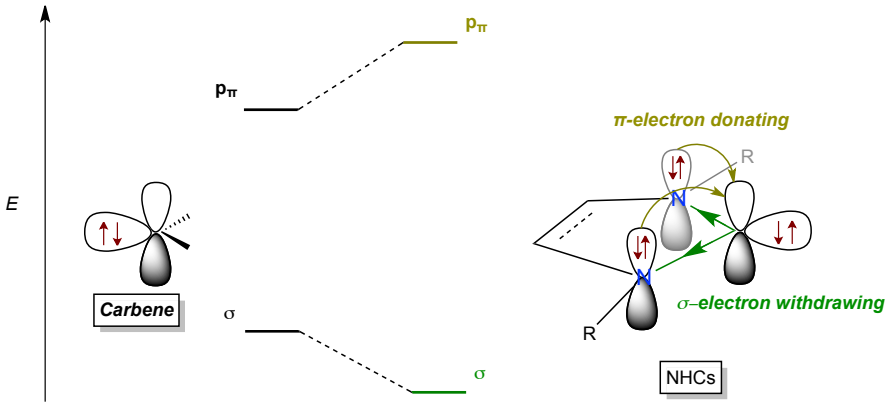


Figure 13. Comparison between energy gaps in a classic singlet carbene and a NHC

The use of bulky substituents, such as adamantyl groups, at the adjacent N atoms is what allowed Arduengo to isolate the first "*bottleable*" carbene, IAd (IAd = 1,3-bis(adamantyl)imidazol-2-ylidene) (Figure 14).[68]

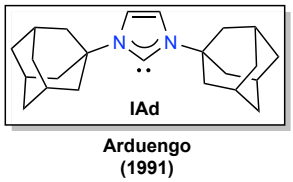


Figure 14. First "*bottleable*" carbene: IAd

During the last two decades, the use of NHCs has become a very popular field of study and numerous applications have been found. The most notable is their application as ancillary ligands in organometallic chemistry,[4,69] however their use as organocatalysts has also become very popular.[70]

As a result of their pioneering work on the field of NHCs, Wanzlick[71] and Öfele[72] independently reported in 1968 the first metal complexes bearing NHCs as ancillary ligands (Figure 13).

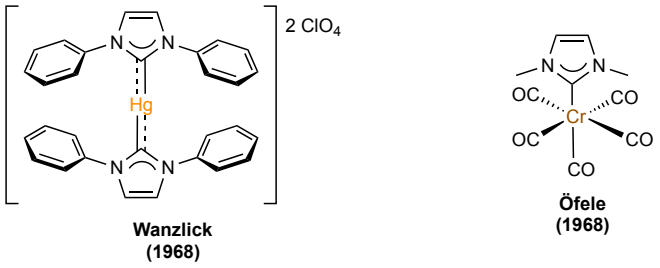


Figure 13. First M-NHC complexes reported by Wanzlik and Öfele

However, it was not until Arduengo reported the synthesis and isolation of IAd, that a real breakthrough was seen in this field.[68] Since then, NHCs have become increasingly popular as an alternative to classical ancillary ligands,[4,69] such as phosphines or cyclopentadienyls,[73] in organometallic chemistry. This popularity arises from the great stability that NHC ligands confer to metal complexes, which comes from their electronic and steric properties.

1.2.1 *Electronic Properties*

There are several metrics to quantify the electronic properties of NHC as ancillary ligands. However, as the Tolman Electronic Parameter (TEP) is the most common and allows a direct comparison with phosphine ligands, it will be the focus of this briefing. If the reader is interested in a more detailed discussion about alternative metrics, we recommend a recent review on this topic by Nelson *et al.*[74]

Since at the beginning NHCs were seen as mere phosphine mimics, the "Tolman Electronic Parameter" (TEP),[75] which was originally developed to describe the electronic properties of the latter, was rapidly adopted as the standard metric to measure the electronic richness of NHCs. Moreover, the use of the TEP as metric allowed a direct comparison between the electronic properties of NHCs and phosphines as ancillary ligands.

In metal-carbonyl complexes, such as $[Ni(CO)_3(L)]$, bearing either NHC or phosphine ligands, the electron density of the ancillary ligand can pass towards the metal centre on to the π^*_{CO} anti-bonding orbital, thus modifying the CO stretching frequency ($\tilde{\nu}_{CO}$) in the IR spectrum (Figure 14).[75] Increasing the electron density on the metal will strengthen the M-C bond through π-donation into the π^*_{CO} anti-bonding orbital, thus weakening the C≡O bond. On the other hand, if the electron density is reduced, this will weaken the M-C bond and strengthen the C≡O bond.[75] Therefore, the electronic properties of the ligand can be easily deduced from the IR spectrum: the lower the $\tilde{\nu}_{CO}$, the stronger the electron donating ability of

the ligand. Comparison between TEPs for NHCs and phosphines revealed that, in general, NHCs are better electron-donor ligands than phosphines (Figure 14).

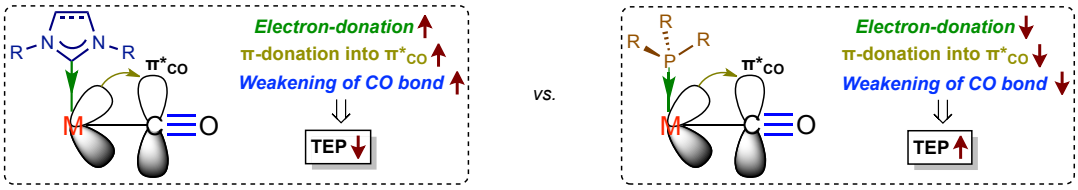


Figure 14. Comparison between the TEP for NHCs and phosphines.

Until recently, the most common carbonyl complexes used to measure TEPs were $[Ni(CO)_3(L)]$ (L = NHC or PR_3). However, due to the high toxicity and in some cases instability of these Ni complexes, they have started to be replaced by Ir and Rh-carbonyl species, such as $[MCl(CO)_2(L)]$ (M = Rh or Ir, L = NHC or PR_3) (Figure 15).[67a,76] It is possible to interconvert the TEPs obtained from the different carbonyl species (Ni, Rh, Ir) into each other, in order to allow comparison between them (Figure 15).[67a,74] It is worth noting that the data can only be compared if the IR measurements have been taken in the same manner; i.e. the same solvent is used. Otherwise, the stretching frequencies can vary significantly and therefore lead to wrong conclusions.[67a,74]

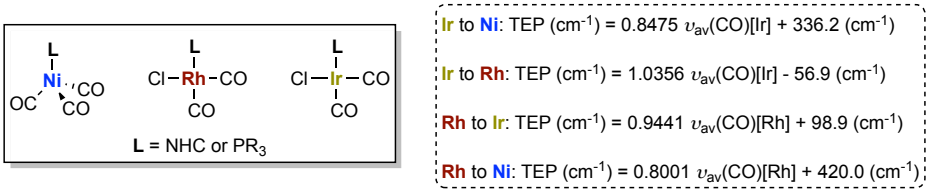


Figure 15. Carbonyl systems used to determined TEPs

The TEP provides a measurement of the ability of the metal to donate electron density into the π^* orbital but does not give any information on the nature of the M-NHC bond, which can be quite complex.[77] NHCs commonly behave as σ-donor/π*-acceptor ligands. As the M-L bond is mostly due to the M←L σ-contribution, the M-NHC bonds are stronger than the analogous M-PR_3 bonds. Even if the π-interactions are not as significant as the σ-donation in the M-NHC bond, they cannot be neglected. The π-interactions are classified as: a) M→NHC π*-backdonation from the *d*-orbitals of the metal to the π*-orbitals of the NHC and b) in the case of electron deficient metals, M←NHC π-donation from a combination of filled and empty π-orbitals of the NHC to the *d*-orbital of the metal (Figure 16). [77a]

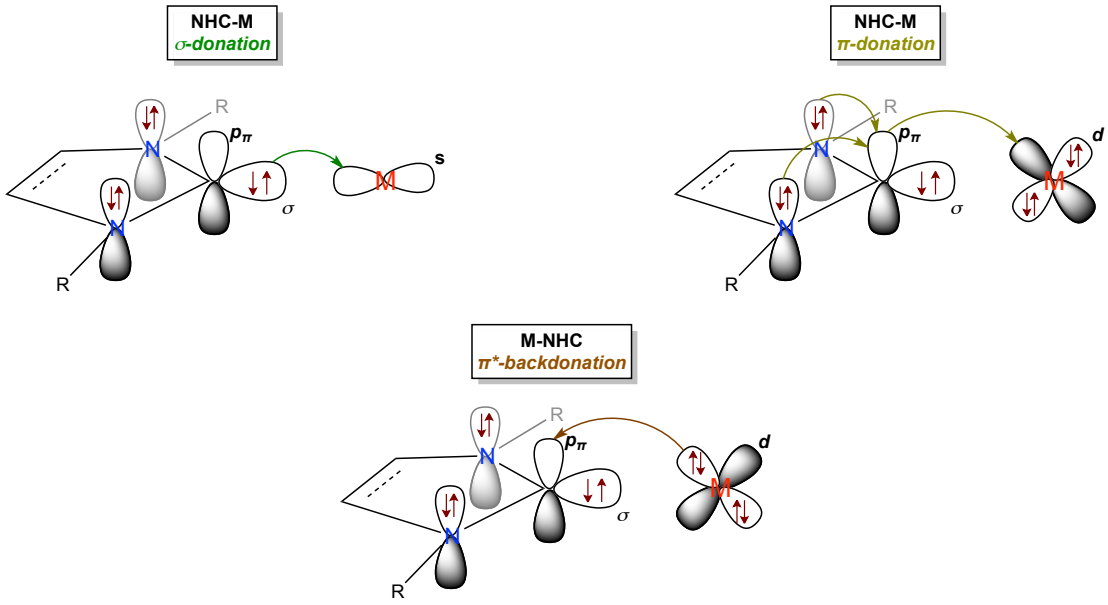


Figure 16. σ and π interactions on the M-NHC bond.

1.2.2 *Steric Properties*

Although NHC ligands have been seen as phosphine mimics and the Tolman electronic parameter can be used to determine their electronic properties, when it comes to the steric hindrance, "Tolman's cone angle",[75] which measures the steric demand of phosphine ligands, has proven to be unfeasible for the description of the steric hindrance offered by NHCs. This is due to the different shapes of both types of ligands. While phosphines present an inverted conical shape, NHCs can be described as having an umbrella type conformation. To solve this problem, Cavallo *et al.* developed and refined the "*buried volume*" ($\%V_{Bur}$),[78] allowing a better comparison between ligands.[79] The $\%V_{Bur}$ is the percentage of volume of the first coordination sphere around the metal occupied by a certain ligand (Figure 17).[78a]

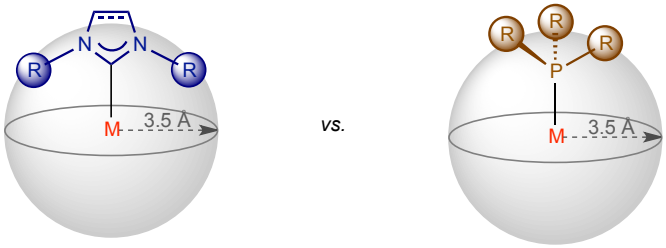


Figure 17. Representation of [M(L)] coordination sphere with NHCs and phosphines.

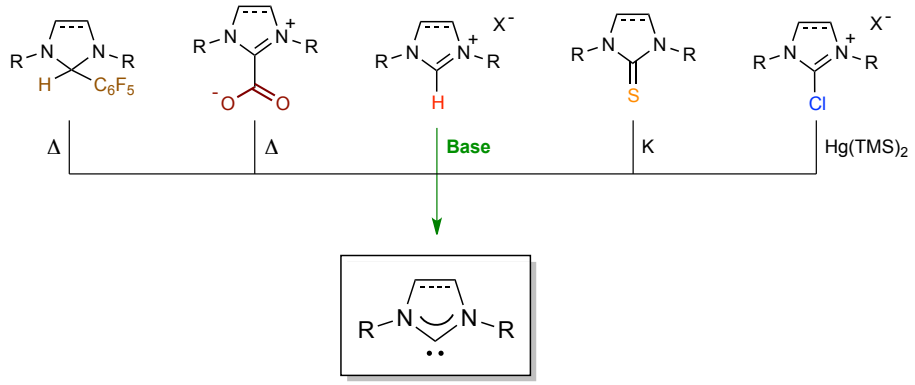
Care should be taken when interpreting and comparing $\%V_{Bur}$. To prevent inconsistencies, it is recommended to compare $\%V_{Bur}$ for NHCs bound to the same metal centre and calculate the values using the same parameters.[79] The $\%V_{Bur}$ values are obtained from solid-state crystal structures, therefore might not be completely representative of the actual coordination

environment a metal centre experiences in solution. Therefore, the $\%V_{Bur}$ values should be used to represent a trend rather than an absolute number and in any case should be interpreted with caution.

In addition to their interesting steric and electronic properties, another reason why NHCs have become so popular is their ease of synthesis and modification, which provides straightforward access to a wide library of ligands.[80] Moreover, it is possible to selectively tune the electronic or steric properties on NHC ligands.

1.2.3 *Synthesis of NHCs*

The most common methodology for the formation of NHCs uses imidazolium and imidazolidinium salts as starting materials, as these species can be easily deprotonated in the presence of a suitable base, such as NaH or K^{t}OBu.[69b,80] There are more procedures available in the literature, *e.g.* decarboxylation, desulfurisation or α-elimination of a suitable leaving group, but their use is not as widespread as the deprotonation approach (Scheme 27).[68b]



Scheme 27. Available pathways for the formation of the free carbene

There are two main strategies for the synthesis of imidazolium and imidazolidinium salts: a) ring closure reaction from a backbone precursor or b) ring closure reaction from a formamidine precursor (Figure 18).[80]

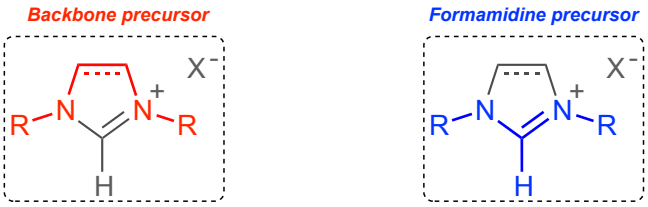
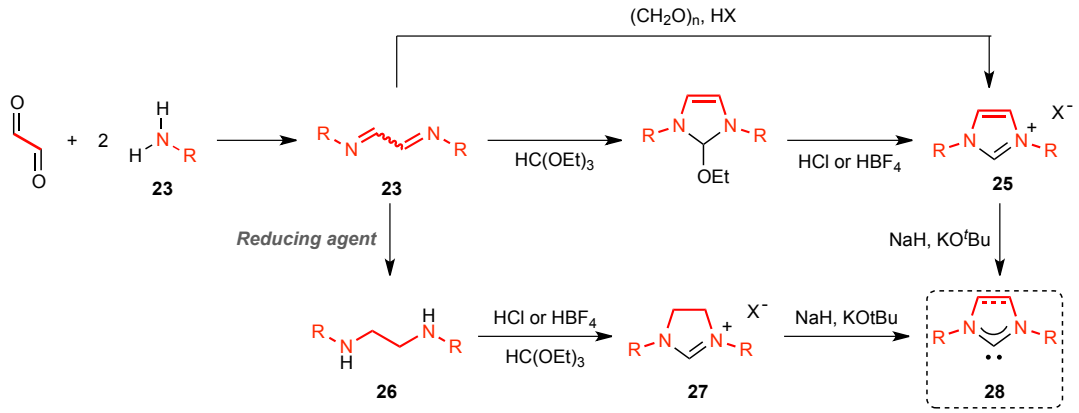


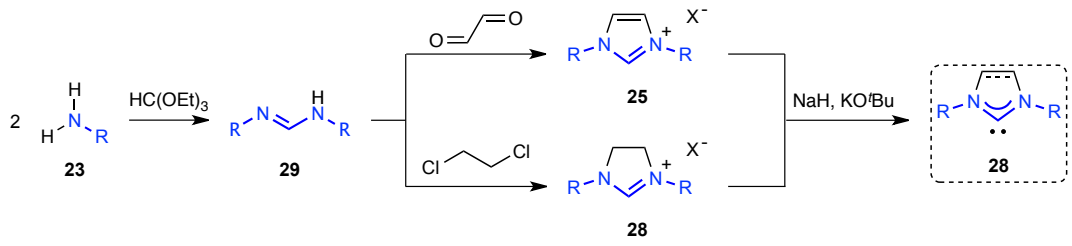
Figure 18. Main strategies for the synthesis of NHC salts

In the first strategy, the backbone precursor is formed by reacting 2 equiv. of a given amine (**23**) with 1 equiv. of glyoxal to obtain the 1,4-diaza-1,3-butadiene (**24**), and then use a C_1 building-block (formaldehyde or $HC(OEt)_3$) to form an imidazolium salt (**25**). By reducing **24**, forming the diamine **26**, before the ring closure step it is possible to access imidazolidinium salts (**27**). Then both **25** or **27** can be deprotonated with an excess of NaH and submolecular amounts of KO^{t}Bu, generating the desired NHC **28** (Scheme 28).[80]



Scheme 28. Synthesis of NHCs by ring closure of a backbone precursor

The second strategy consists of the formation of a formamidine precursor (**29**), by reacting 2 equiv. of a given amine **23** with 1 equiv. of ethyl orthoformate, which will react with glyoxal during the ring closure step (Scheme 29).[80] In 2008, Grubbs and co-workers reported an alternative procedure for the formation of imidazolidinium salts (**27**) consisting of the reaction of 1,2-dichloroethane with the corresponding formamidine **29** (Scheme 29).[81] Afterwards the imidazolium salt is deprotonated as previously described in order to afford the desired NHC **28**.



Scheme 29. Synthesis of NHCs from a formamidine (**29**) precursor.

The use of Au-NHC complexes in homogenous gold catalysis has become very popular field of study during the last 10 years. The work described in the following chapters represents a small contribution towards a better understanding of the reactivity of these

fascinating complexes and the intermediate species involved during gold-catalysed transformations.

2. The Influence of a Very Bulky *N*-Heterocyclic Carbene in Gold Catalysis

2.1 Introduction

As seen in Chapter 1, during the last few years the use of *N*-heterocyclic carbenes (NHCs) as ancillary ligands in gold complexes has gained increased attention, as they provide unique properties such as unprecedented σ-donation and significant steric bulk.[5] Further advantages offered by NHC ligands, in practical terms, are their ease of synthesis and modification, providing access to a wide range of [Au(NHC)Cl] complexes.[82] Among them, IPr has emerged as the ligand of choice for a vast number of transformations catalysed by gold-NHC complexes. This is due to the unique combination of steric and electronic properties offered by this particular ligand. Therefore, in an attempt to obtain ever more active catalysts, several research groups have investigated how to modify the electronic and steric properties of this privileged architecture.[67a]

Recently, Markó *et al.* reported the synthesis of IPr* (**1**) (IPr* = 1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazol-2-ylidene),[83] inspired by the NHCs with "flexible sterics" described by Glorius[84] and Bertrand[85] (Figure 1).

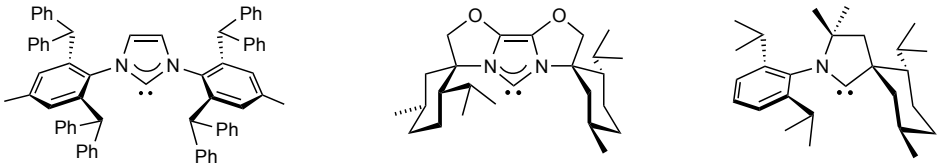


Figure 1. Examples of bulky-yet-flexible NHC ligands.

This new NHC was found to be an extraordinarily sterically bulky ligand, with a $\%V_{Bur}$[78a,79,86] of 53.6 calculated for [Ag(IPr*)Cl][83] (**2**) and also exhibits good electron-donating capability (TEP = 2052.7 cm^{-1}).[87] However, to the best of our knowledge, the IPr* ligand had only been employed in the synthesis of [Ag(IPr*)Cl], [Rh(IPr*)$(CO)_2$Cl] and [Rh(acac)(IPr*)(CO)] complexes.[83] Moreover, no catalytic studies had been performed to evaluate its role in metal catalysed organic reactions. Intrigued by the steric and electronic properties of this bulky ligand, we decided to study its effect on the catalytic activity of Au^I-complexes.

2.2 Results and discussion

2.2.1 *Synthesis and Characterization*

[Au(NHC)Cl] complexes are generally synthesised using three different routes: a) transfer of the NHC ligand from a silver complex;[82a] b) the recently disclosed method involving transmetallation from copper-NHC complexes[88] or c) by direct reaction of a free carbene with a gold(I)-precursor (Scheme 1).[82a] Since Markó reported the failure of the silver complex **2** as a transmetallation agent but did not specify with what metals the reaction was tested,[83] the transmetallation between [Ag(IPr*)Cl] and [Au(SMe_2)Cl] was attempted in order to synthesise [Au(IPr*)Cl] (**C1**). Unfortunately, the formation of the desired gold complex was not observed (route A, Scheme 1). As the transmetallation with silver is also invalid for gold, [Cu(IPr*)Cl] (**3**) was then tested as NHC transfer agent. Copper complex **3** was easily obtained as a white crystalline material, following the literature protocol for the synthesis of [Cu(NHC)Cl] complexes,[89] in 98% yield. Crystals suitable for single crystal diffraction studies were obtained. A thermal ellipsoid representation of complex **3** is presented in Figure 2. Unfortunately, the transmetallation between **3** and [Au(SMe_2)Cl] was also ineffective (route B, Scheme 1). This is, as in the case of silver, presumably due to the steric bulk of the IPr* ligand.

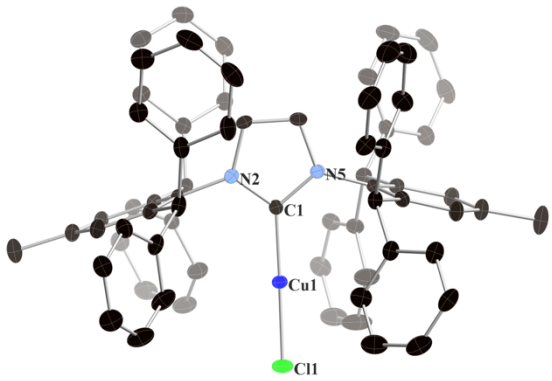
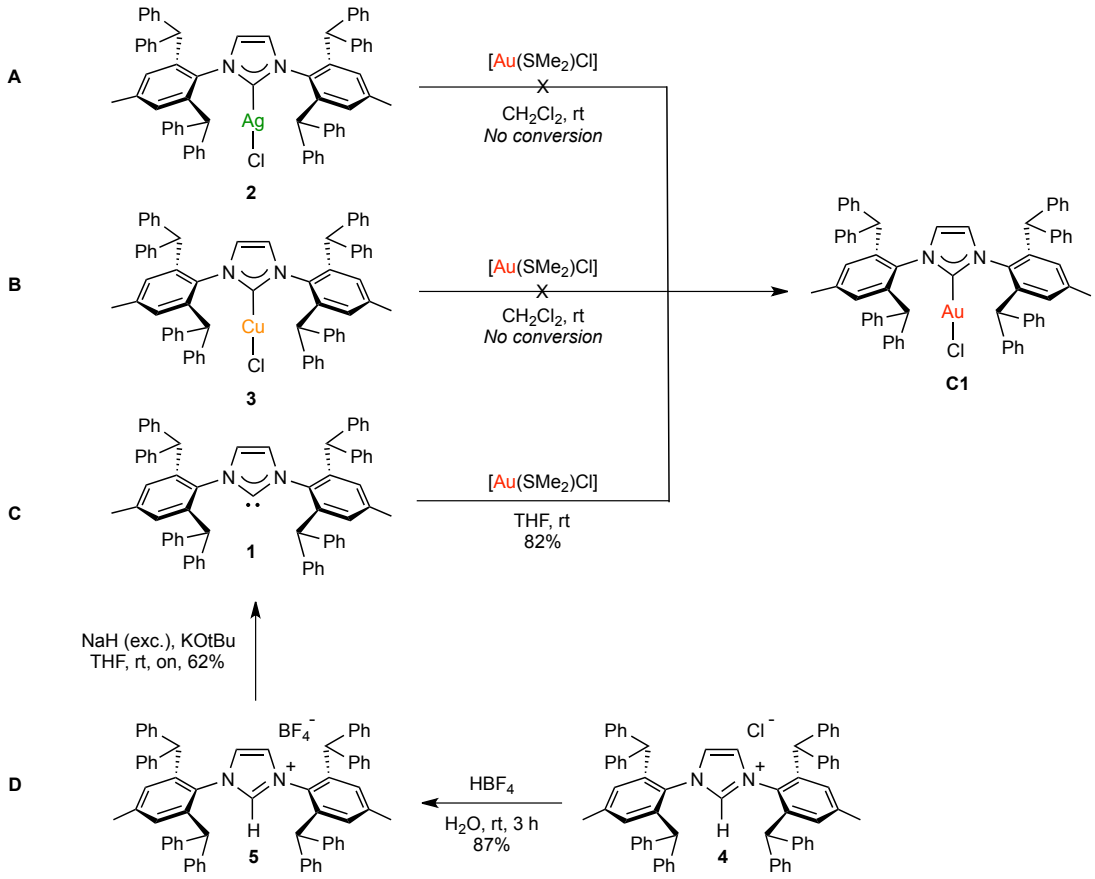


Figure 2. Thermal ellipsoid representation for [Cu(IPr*)Cl] (**3**) showing 50% thermal ellipsoids probability. H atoms were omitted for clarity purposes. Selected bond distances (Å) and angles (º): Cu1-C1 1.867(3), Cu1-Cl1 2.0944(9), C1-N2 1.351(4), C1-N5 1.364(4), C1-Cu1-Cl1 176.21(9), N2-C1-N5 103.8(2).

The synthesis of [Au(IPr*)Cl] (**C1**) was next attempted by reacting the free carbene (**1**) and [Au(SMe_2)Cl] (route C, Scheme 1). Noteworthily, our optimised standard procedure for the synthesis of free NHC ligands involves the use of the corresponding BF_4 salt, therefore IPr*•HCl (**4**)[83] was first reacted with aq. HBF_4 affording IPr*•HBF_4 (**5**) in 87% yield (route D, Scheme 1). A significant upfield shift of the imidazolium proton was observed by ^{1}H NMR spectroscopy, shifting from 12.95 to 10.13 ppm in $CDCl_3$. Crystals suitable for single

crystal diffraction studies were obtained by slow diffusion, at -20 ºC, of pentane into a saturated dichloromethane solution of **5** (Figure 3).



Scheme 1. Synthetic approaches towards [Au(IPr*)Cl] (**C1**)

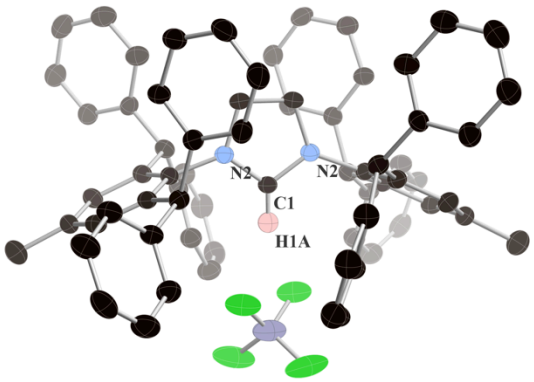


Figure 3. Thermal ellipsoid representation for IPr*•HBF4 (**5**) showing 50% thermal ellipsoids probability. H atoms, except from the imidazolium proton, were omitted for clarity purposes. Selected bond distances (Å) and angles (º): C1-N2 1.337(4), C1-N2 1.337(4), N2-C1-N2 108.1(4).

IPr*•HBF_4 **5** was then deprotonated in the presence of a slight excess of NaH and a catalytic amount of KO^{t}Bu, to afford carbene **1** as a white powder in 62% yield (route D,

Scheme 1). After recrystallisation of the free NHC ligand, **1** was reacted with [Au(SMe_2)Cl]. Gratifyingly, the desired gold complex [Au(IPr*)Cl] (**C1**) was obtained in 82% yield (route C, Scheme 1). Crystals suitable for single crystal diffraction studies were obtained by slow diffusion, at -20 ºC, of pentane into a saturated dichloromethane solution of **C1** (Figure 4). As expected **C1** is a linear complex with a C1-Au1-Cl1 angle of 178.3(2)º and the Au1-C1 bond length of 1.987(7) Å. The Au1-C1 bond length is longer than the corresponding bond in Au-complexes bearing IPr (1.942(3) Å) or SIPr (1.979(3) Å) ligands, but within the normal range for [Au(NHC)Cl] complexes.[82a]

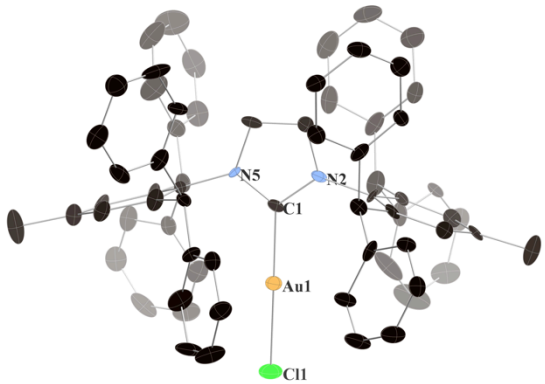


Figure 4. Thermal ellipsoid representation for [Au(IPr*)Cl] (**C1**) showing 50% thermal ellipsoids probability. H atoms were omitted for clarity purposes. Selected bond distances (Å) and angles (º): Au1-C1 1.987(7), Au1-Cl1 2.274(2), C1-N2 1.332(9), C1-N5 1.347(9), C1-Au1-Cl1 178.3(2), N2-C1-N5 106.3(6).

Computational studies using Samb*V*ca[90] software revealed that the $\%V_{Bur}$ of IPr* for [Au(IPr*)Cl] **C1** (50.4), and [Cu(IPr*)Cl] **3** (50.1), are smaller than that calculated for [Ag(IPr*)Cl] **2** (53.5).[83,91] The variation of $\%V_{Bur}$ of IPr* with different metals can be explained by the flexibility of the ligand, allowing it to adapt its shape to the coordination environment around the metal centre. These results also explain the different $\%V_{Bur}$ for [Au(IPr*)Cl] calculated by us, in comparison to values provided by Glorius in his recent review on NHCs,[67a] which were calculated using the closely related [Ag(IPr*)Cl] complex. At the time of this study the honorific title of "bulkiest NHC" based on $\%V_{Bur}$ still belonged to the CAAC ligand reported by Bertrand *et al.* with a $\%V_{Bur}$ of 51.2 (Figure 1).[92] However, since then several bulkier NHC ligands have been reported, e.g. 7-DIPP, IPr** and IPr*$^{(2\text{-Np})}$ (Figure 5).[93] To prevent inconsistencies, it is recommended to compare $\%V_{Bur}$ for NHCs bound to the same metal centre and calculate the values using the same parameters.[79] The $\%V_{Bur}$ values are obtained from solid-state crystal structures, therefore might not be completely representative of the actual coordination environment a metal centre experiences in solution. The $\%V_{Bur}$ values should therefore be used to represent a trend rather than an absolute number and in any case should be interpreted with caution.

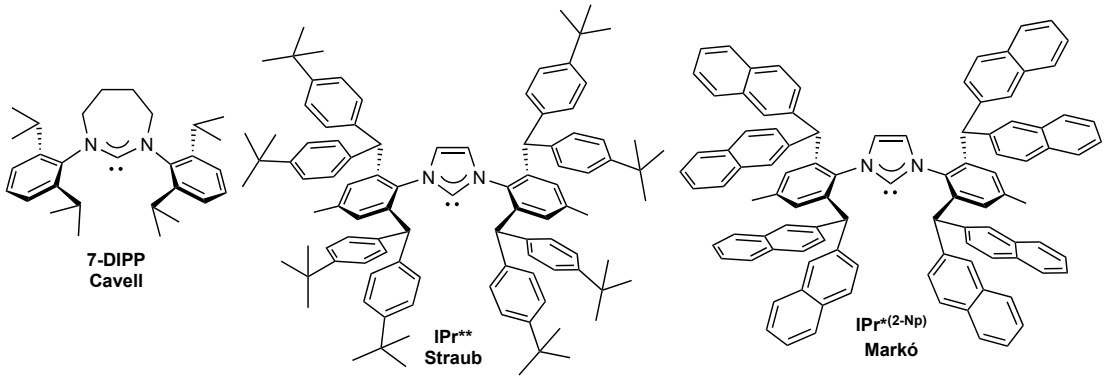
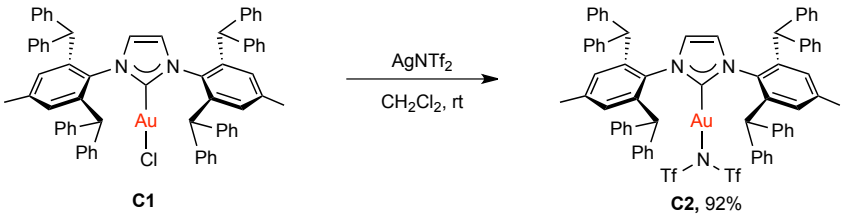


Figure 5. Highly sterically demanding NHC ligands reported after IPr*

As mentioned in Chapter 1, silver salts are generally hygroscopic, expensive, light sensitive and present unpredictable catalytic activity, therefore some protocols have been reported for Au-catalysed organic reactions in the absence of silver additives.[22a,25,27a,29] The air stable [Au(NHC)(NTf_2)] complexes, reported by Gagosz,[22a] represent a very attractive and practical alternative to the use of protocols involving a silver co-catalyst. Thus, the synthesis of [Au(IPr*)(NTf_2)] (**C2**) was also attempted following the established procedure.[22a] Gratifyingly, the desired complex was isolated in 92% yield as a white microcrystalline solid (Scheme 2). Crystals suitable for X-ray diffraction analysis were obtained (Figure 6).



Scheme 2. Synthesis of [Au(IPr*)(NTf_2)] (**C2**)

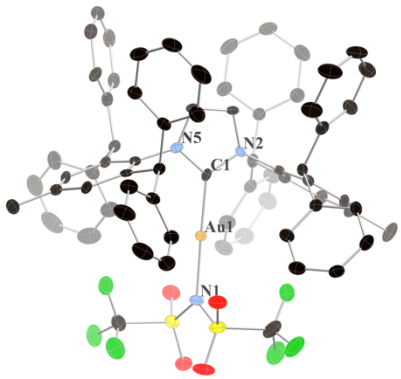


Figure 6. Thermal ellipsoid representation for [Au(IPr*)(NTf_2)] (**C2**) showing 50% thermal ellipsoids probability. H atoms were omitted for clarity purposes. Selected bond distances (Å) and angles (°): Au1-C1 1.986(7), Au1-N1 2.086(6), C1-N2 1.344(9), C1-N5 1.357(9), C1-Au1-N1 178.2(3), N2-C1-N5 105.9(6).

As expected **C2** is a linear complex with a C1-Au1-Cl1 angle of 178.2(3)º and a Au1-C1 bond length of 1.986(7) Å. The latter is longer than the corresponding bond in Au-complexes bearing IPr (1.969(2) Å) or IMes (1.976(3) Å) ligands, but within the normal range for [Au(NHC)(NTf_2)] complexes.[22a] As expected the $\%V_{Bur}$ of IPr* for **C2** (44.8) is smaller than for **C1** (50.1). This can be explained by the steric bulk of the ligand *trans* to the carbene, which is more significant for NTf_2 than for Cl.

2.2.2 *Catalytic studies*

Next, the catalytic activities of **C1** and **C2** were evaluated in several organic transformations known to be catalysed by bulky gold-NHC complexes, such as the tandem alkoxylation/lactonisation of γ-hydroxy-α,β-acetylenic esters,[94] the [3,3]-rearrangement of propargylic acetates leading to the formation of conjugated enones[40,95] and substituted indenes,[30b,96] as well as the rearrangement of allylic acetates.[97] In order to get a better understanding of the influence of the steric hindrance around the gold centre, the reactivity of **C1** and **C2** was compared to a range of Au-NHC complexes. Their structures and corresponding $\%V_{bur}$ can be found in Figure 7. For practical reasons, and to avoid the use of silver salts, whenever possible the catalyst screening was carried our using [Au(NHC)(NTf_2)] complexes.

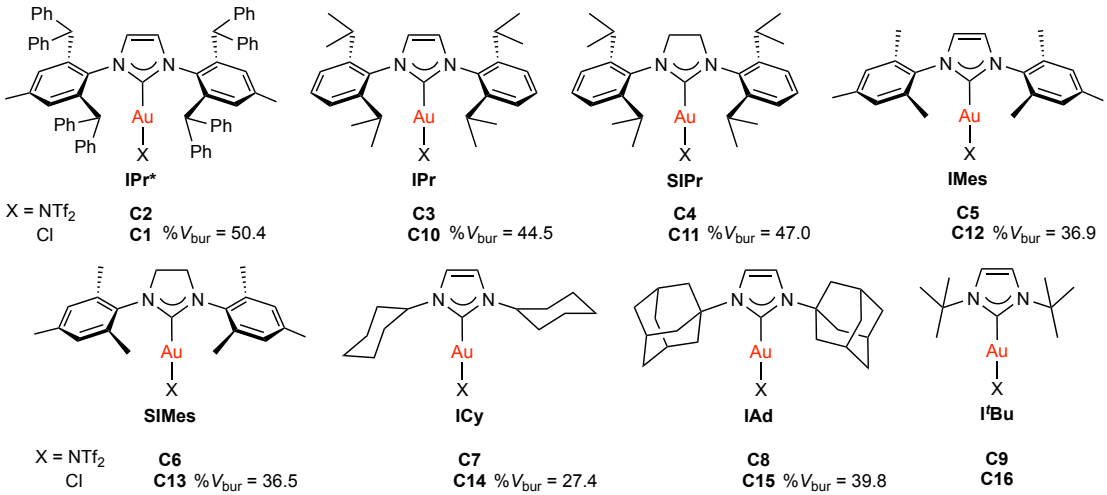


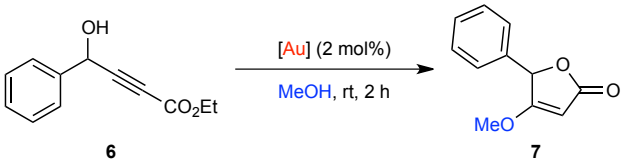
Figure 7. Au-complexes used in the catalytic studies and their corresponding $\%V_{bur}$.

2.2.2.1 *Gold-catalysed formation of furanones*

We have recently reported the base-free gold-catalysed formation of several 4-alkoxy-2(*5H*)-furanones from a variety of propargylic alcohols using a simple and straightforward procedure consisting of the use of **C3** (2 mol%) in MeOH at room temperature to afford the desired furanones in good yields (48-98%).[94] Therefore we thought that this was a good

reaction to test the catalytic activity of [Au(IPr*)(NTf_2)]. However, initial studies revealed that the formation of furanone **7** is favoured when using small NHC ligands (Table 1). Complexes **C8** and **C9** afforded compound **7** in very good conversions (Entries 6 and 7; Table 1) while **C3** and **C4** afforded moderate conversions (Entries 2 and 3; Table 1). For the reaction catalysed by **C5** and **C6** no conversion could be determined, due to the complexity of the mixture obtained (Entries 4 and 5; Table 5). As expected after the initial screening, **C2** showed poor catalytic activity for this transformation, allowing only 18% conversion to the desired furanone **7** (Entry 1; Table 1). In addition to the higher steric hindrance around the metal centre, this result could also be attributed to the poorer solubility of [Au(IPr*)(NTf_2)] in the reaction media compared to the other catalysts.

Table 1. Catalyst screening for the synthesis of furanone **7**[a]



6 **7**

Entry	Catalyst	Conversion (%)[b]
1	[Au(IPr*)(NTf_2)] (**C2**)	18
2	[Au(IPr)(NTf_2)] (**C3**)	67
3	[Au(SIPr)(NTf_2)] (**C4**)	45
4	[Au(IMes)(NTf_2)] (**C5**)	nd
5	[Au(SIMes)(NTf_2)] (**C6**)	nd
6	[Au(IAd)(NTf_2)] (**C8**)	85
7	[Au(I^{t}Bu)(NTf_2)] (**C9**)	83

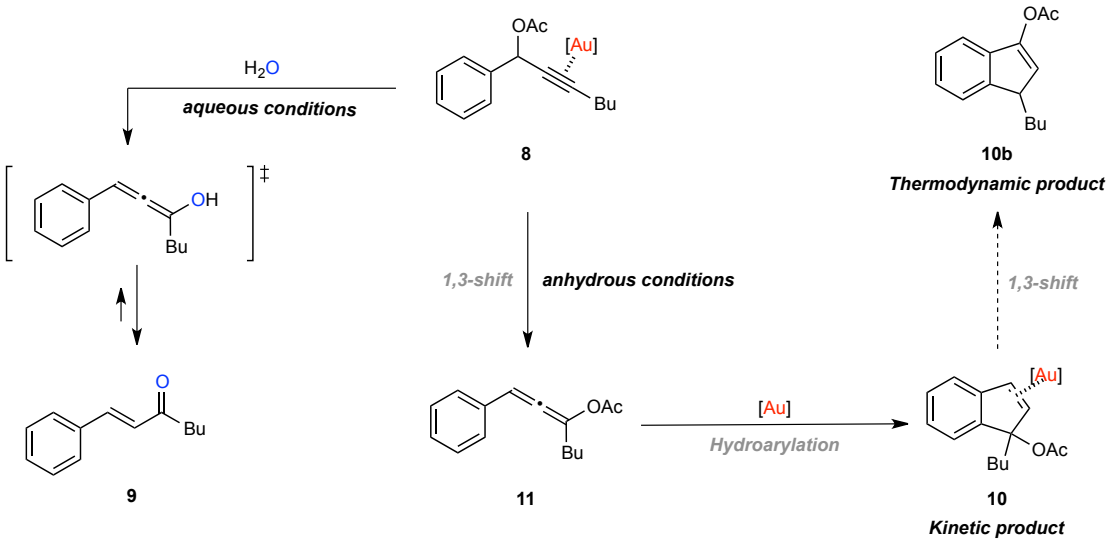
[a] Reaction conditions: propargylic alcohol **6** (0.24 mmol), [Au] (2 mol%), MeOH (2 mL). [b] Conversions determined by ^{1}H NMR as an average of 2 runs. [c] nd= not determined. Along with the desired product various side products were observed.

2.2.2.2 Gold-catalysed isomerisation of propargylic acetates into enones and indenes

The activity of gold(I) complexes **C1** and **C2** in the rearrangement of propargylic acetates was also studied. The rearrangement of propargylic acetate **8** can afford four different compounds depending on reaction conditions: a) α,β–unsaturated ketone **9** under aqueous conditions,[40,95] b) substituted indenes **10** (kinetic product)[7a] or **10b** (thermodynamic product) under anhydrous conditions[26] and c) depending on the gold complex, the reaction could be stopped at the allene **11** (Scheme 5).[30e]

Our group[40] and Zhang and coworkers,[95] have independently reported the isomerization of **8** into **9** under mild conditions. Taking into account our reported catalytic protocol,[40] the reaction procedure was slightly modified to study the activity of [Au(NHC)(NTf_2)] at shorter

reaction times, allowing better comparison between catalysts (Table 2). In contrast to our previous results using [Au(NHC)Cl] complexes activated by $AgSbF_6$,[40] [Au(NHC)(NTf_2)] complexes furnished diminished yields of enone **9** (*e.g.* 98% with [Au(I^{t}Bu)Cl]/$AgSbF_6$ to 89% with [Au(I^{t}Bu)(NTf_2)]).



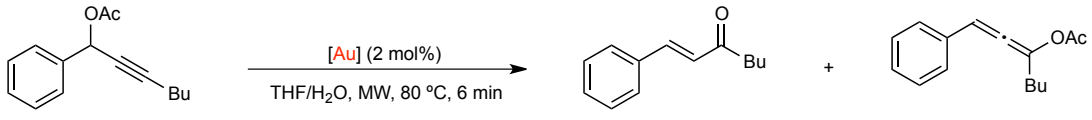
Scheme 5. Rearrangement of propargylic acetates into conjugated enones, substituted indenes or allenes.

Initial optimisation studies indicated that complexes bearing sterically demanding NHC ligands afforded **9** in better yields than complexes bearing smaller ones. Thus, **C3** and **C4** afforded enone **9** in high yields (Entries 2 and 3; Table 2) while **C5-C8** provided only moderate yields (Entries 4-7; Table 2). Complex **C9** was the best for this transformation affording an excellent 89% yield. However, no logical explanation based on steric or electronic parameters could be found. Unfortunately, rearrangement of propargylic acetate **8** in the presence of **C2** furnished disappointing conversions (Entry 1; Table 2).

A possible solvent effect was considered as the source of the problem, due to the ability of THF to coordinate to the gold centre.[98] The reaction was therefore tested in benzene and 1,2-dichloroethane (DCE). In both cases a remarkable increase in the yield of **9** was observed (Entries 3 and 5; Table 3). Noteworthily, reactions in benzene furnished a significant increase of allene **11** (Entries 3 and 4; Table 3). The selective formation of allenes and inhibition of subsequent gold catalysed transformations was already reported by our group to be strongly dependent on the labile ligand attached to the gold centre. Allene **11** was selectively formed in the gold-catalysed rearrangement of propargylic acetate **9** applying several [Au(NHC)(L)][BF_4] complexes, with L = nitrogen-based ligand.[30e] A similar effect induced by benzene acting as a labile ligand to stabilise the cationic gold centre in the reaction mixture may rationalise the analogous observations in the current case. Finally, **C2** performed better

than **C3** (Entries 5 and 6; Table 3) for reactions carried out in DCE. These results strongly support the hypothesis of coordinating solvents dampening the catalytic activity of **C2**, due to the effective steric protection of the gold centre by both the NHC ligand and the solvent, resulting in no coordination of substrate to the catalyst (see Entries 1, 3 and 5; Table 3). The use of coordinating solvents was therefore avoided in the following reactions.

Table 2. Catalyst screening for the isomerization of propargylic acetate **8** into α,β–unsaturated ketone **9**[a]

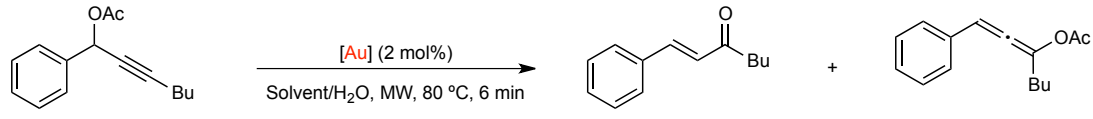


8 **9** **11**

Entry	Catalyst	9 (%)[b]	10 (%)[b]
1	[Au(IPr*)(NTf$_2$)] (**C2**)	8	18
2	[Au(IPr)(NTf$_2$)] (**C3**)	79	17
3	[Au(SIPr)(NTf$_2$)] (**C4**)	83	13
4	[Au(IMes)(NTf$_2$)] (**C5**)	38	33
5	[Au(SIMes)(NTf$_2$)] (**C6**)	61	24
6	[Au(ICy)(NTf$_2$)] (**C7**)	40	32
7	[Au(IAd)(NTf$_2$)] (**C8**)	51	28
8	[Au(I^{t}Bu)(NTf$_2$)] (**C9**)	89	7

[a] Reaction conditions: propargylic acetate **8** (0.22 mmol), [Au] (2 mol%), THF (2 mL), H_2O (0.2 mL). [b] Yields determined by ^{1}H NMR as an average of at least 2 runs.

Table 3. Solvent influence on the catalyst activity[a]



8 **9** **11**

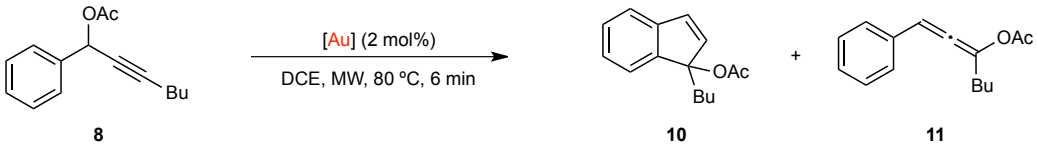
Entry	Solvent	Catalyst	9 (%)[b]	11 (%)[b]
1	THF	[Au(IPr*)(NTf2)] (**C2**)	8	18
2	THF	[Au(IPr)(NTf2)] (**C3**)	79	17
3	Benzene	[Au(IPr*)(NTf2)] (**C2**)	23	67
4	Benzene	[Au(IPr)(NTf2)] (**C3**)	48	32
5[c]	DCE	[Au(IPr*)(NTf2)] (**C2**)	78	0
6[c]	DCE	[Au(IPr)(NTf2)] (**C3**)	65	0

[a] Reaction conditions: propargylic acetate **8** (0.22 mmol), [Au] (2 mol%), solvent (2 mL), H_2O (0.2 mL). [b] Yields determined by ^{1}H NMR as an average of at least 2 runs. [c] Indene **10** was found in 22% yield in Entry 5 and 31% yield in Entry 6.

Our group also reported the [3,3]-rearrangement/intramolecular hydroarylation of propargylic acetate **8** into indene **10**.[30b,96] In these studies, the conversion of the standard substrate **8** into indene **10** was accomplished in good yields after 5 min in CH_2Cl_2 using

[Au(IPr)Cl)]/$AgBF_4$ (2 mol%) as the catalytic system. Initial studies revealed that complex **C2** was unsuitable for this transformation, as the hydroarylation of **11** does not occur under these reaction conditions. However, we observed formation of **10** under microwave irradiation in the presence of **C2** during the synthesis of enones from propargylic acetates (see Entries 5 and 6; Table 3). Encouraged by these results, we decided to achieve the transformation of propargylic acetate **8** into indene **10** using microwave irradiation. Anhydrous DCE was used in order to avoid competing enone formation. The catalyst screening revealed the superiority of complexes bearing bulky NHCs (Entries 1, 2, and 3; Table 4). Good yields were obtained with catalysts **C2-C4** (72-85%) while poor yields were obtained with gold-catalysts bearing less sterically demanding NHC ligands (3-45%).

Table 4. Catalyst screening for the synthesis of substituted indenes **10**[a]



8 **10** **11**

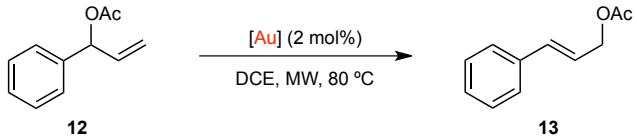
Entry	Catalyst	10 (%)[b]	11 (%)[b]
1	[Au(IPr*)(NTf_2)] (**C2**)	72	11
2	[Au(IPr)(NTf_2)] (**C3**)	85	0
3	[Au(SIPr)(NTf_2)] (**C4**)	79	0
4	[Au(IMes)(NTf_2)] (**C5**)	3	10
5	[Au(SIMes)(NTf_2)] (**C6**)	8	28
6	[Au(ICy)(NTf_2)] (**C7**)	5	50
7	[Au(IAd)(NTf_2)] (**C8**)	17	35
8	[Au(I^{t}Bu)(NTf_2)] (**C9**)	45	23

[a] Reaction conditions: propargylic acetate **8** (0.22 mmol), [Au] (2 mol%), DCE (2 mL). [b] Yields determined by ^{1}H NMR as an average of at least 2 runs. Formation of enone **9** (*E* and *Z*) due to the presence of water was observed.

2.2.2.3 [3,3]-rearrangement of allylic acetates

Finally, the rearrangement of allylic acetates was tested in order to study the potential of the new catalysts in reactions beyond alkyne activation. This classical skeletal rearrangement has been described to be catalysed by several transition metals,[99] including gold.[97] Our group reported in 2007 that a combination of [Au(IPr)Cl] (3 mol%) and $AgBF_4$ (2 mol%) could afford complete rearrangement of **12** into **13** after 12 min at 80 ºC in DCE using microwave irradiation.[97] Initial catalytic studies revealed that this rearrangement was not promoted by [Au(NHC)(NTf_2)] complexes (Table 5). Our group has recently reported the silver free rearrangement of allylic acetates.[29,31b] Therefore, most likely this lack of reactivity might be due to a strong counterion effect for this particular reaction rather than the silver salt acting as a co-catalyst.

Table 5. Catalyst screening of [Au(NHC)(NTf_2)] complexes for the rearrangement of **12**[a]

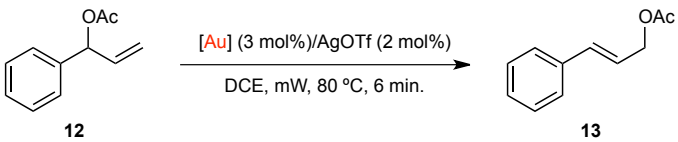


Entry	Catalyst	Times (min)	Conversion (%)[b]
1	[Au(IPr*)(NTf_2)] (**C2**)	6	4
2	[Au(IPr)(NTf_2)] (**C3**)	6	4
3	[Au(IPr*)(NTf_2)] (**C2**)	12	8
4	[Au(IPr)(NTf_2)] (**C3**)	12	8

[a] Reaction conditions: Allylic acetate **12** (0.28 mmol), [Au] 2 mol %, DCE (5 ml). [b] Conversions determined by ^{1}H NMR as an average of 2 runs.

In order to circumvent this lack of reactivity and evaluate how the steric hindrance of the NHC ligand affected the rearrangement of allylic acetates, a combination of [Au(NHC)Cl] and AgOTf was used during the catalyst screening. Moreover, the reaction time was reduced to 6 min to allow a better comparison between the catalysts' activities. As shown in Table 6, **C10** exhibited the best catalytic performance, achieving 84% conversion (Entry 2; Table 6). Unfortunately, **C11** and **C15**, which allowed almost full conversion under the initial conditions, were not very active at shorter reaction times (Entries 3 and 4; Table 6). We were pleased to see that **C1** promoted the reaction in very good conversions (79%), showing similar catalytic activity as **C10**, the best catalyst in our previous report (Entries 1, 2 and 5; Table 6).[97]

Table 6. Catalyst screening for the rearrangement of allylic acetate **12**[a]



Entry	Catalyst	Conversion (%)[b]
1	[Au(IPr*)Cl] (**C1**)	79
2	[Au(IPr)Cl] (**C10**)	84
3	[Au(SIPr)Cl] (**C11**)	55
4	[Au(IAd)Cl] (**C15**)	68
5	[Au(I^{t}Bu)Cl] (**C16**)	76

[a] Reaction conditions: allylic acetate **12** (0.28 mmol), [Au] (3 mol %), AgOTf (2 mol %) DCE (5 mL). [b] Conversions determined by GC as an average of 2 runs.

2.3 Conclusion

To conclude, the syntheses of carbene **1** and complexes [Au(IPr*)Cl] (**C1**) and [Au(IPr*)(NTf_2)] (**C2**) have been performed in high yields. In addition, the $\%V_{bur}$ of IPr* for **C1** and **C2** was evaluated revealing it to be one of the bulkiest NHC ligands on [Au(NHC)Cl] complexes reported to date. The catalytic activity of **C1** and **C2** in several reactions typically catalysed by bulky Au^I-complexes was investigated, displaying a strong solvent effect. Gold complexes bearing IPr* performed better when the reactions were carried out in less coordinating solvents. Although this study showed that [Au(IPr*)(L)] complexes can perform as efficiently as catalyst bearing bulky NHC ligands such as IPr and SIPr under the appropriate reaction conditions, no general claims can be done regarding whether bigger/bulkier NHC ligands are better than small ones for gold catalysis. Meticulous screenings of the reaction conditions, as well as detailed mechanistic studies, are therefore needed in order to find the most suitable catalyst for a given transformation.

After our initial study, IPr* has also been tested on several transition metal complexes, such as ruthenium[87,100] and palladium.[101] While in the case of ruthenium complexes the IPr* ligand did not bring any reactivity advantages, in comparison with the IPr/SIPr analogues, in the case of palladium it has lead to the development of some of the most active cross-coupling catalytic systems reported to date.[101] In summary, all these results highlight the versatile nature of NHC ligands in transition metal complexes. While a given NHC ligand can afford poor catalytic performances on a certain transition metal it can lead to fascinating reactivity on a different one. Therefore, systematic studies on ligand effects on transition metal complexes are highly important. A better understanding of the relationship between ligand and metal would lead to the development of more efficient catalytic systems.

2.4 Experimental Section

Unless otherwise stated all solvents and reagents were used as purchased and all reactions were performed under air. Dry solvents were obtained from a solvent purification system. NMR spectra were recorded on 400 MHz and 300 MHz spectrometers at room temperature in $CDCl_3$. Chemical shifts are given in parts per million (ppm) with respect to TMS. Reactions under microwave irradiation were performed in a single-mode microwave apparatus, producing controlled irradiation at 2450 MHz. Reaction times refer to hold times at the indicated temperature and not total irradiation times with constant cooling *via* propelled air flow at a set power of 200 W. Elemental analyses were carried out by the analytical services of London Metropolitan University. Compounds **2**[83], **4**,[83] **6**[94], **8**[96] and **12**[97] were synthesised according to literature procedures. CCDC 836610 (**3**), 836611 (**5**), 836612 (**C1**), 836613 (**C2**)

contain the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of [Cu(IPr)Cl]* (**3**): In a microwave vial, inside a glovebox (under Ar atmosphere), **4** (0.26 mmol, 250 mg, 1.00 equiv.), Cu_2O (0.17 mmol, 25.0 mg, 0.66 equiv.) were dissolved in anhydrous toluene (1 mL). The vial was then removed from the glovebox and heated in a microwave reactor at 150 °C for 15 min affording a white crystalline solid in solution. The crude product was dissolved in CH_2Cl_2 (10 mL) and filtered through Celite® to remove the excess of Cu_2O. The pad of Celite® was washed with CH_2Cl_2 (3 x 10 mL) and solvent evaporated *in vacuo* affording complex **3** as a white solid (261 mg, 98%). **^{1}H NMR** (300 MHz; CD_2Cl_2): δ 7.16-7.21 (m, 24H, CH_{Ar}), 7.02-7.05 (m, 8H, CH_{Ar}), 6.92 (s, 4H, CH_{Ar}), 6.88-6.91 (m, 8H, CH_{Ar}), 5.87 (s, 2H, CH_{imid}), 5.21 (s, 4H, CHPh$_2$), 2.25 (s, 6H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$): δ 180.7 (C_{carb}), 143.3 (C_{Ar}), 143.0 (C_{Ar}), 141.4 (C_{Ar}), 140.6 (C_{Ar}), 134.6 (C_{Ar}), 130.5 (CH$_{Ar}$), 130.0 (CH$_{Ar}$), 129.7 (CH$_{Ar}$), 129.0 (CH$_{Ar}$), 128.8 (CH$_{Ar}$), 127.1 (CH$_{Ar}$), 127.0 (CH$_{Ar}$), 123.7 (CH$_{imid}$), 51.6 (CHPh$_2$), 21.9 (CH_3). **Anal. Calcd.** for $C_{69}H_{56}ClCuN_2$ (1012.20): C, 81.88; H, 5.58; N, 2.77. Found: C, 81.73; H, 5.44; N, 2.65.

Synthesis of IPr•HBF$_4$* (**5**): To a suspension of **4** (3.95 mmol, 3.75 g, 1.00 equiv.) in water (250 mL), aq. HBF_4 (5.90 mmol, 0.58 mL, 1.50 equiv.) was added. The mixture was stirred for 3 h at room temperature. Then it was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The resulting solid was dissolved in a minimum amount of CH_2Cl_2, precipitated by the addition of Et_2O and collected by filtration to afford **5** (3.39 g, 86%) as an off-white powder. **^{1}H NMR** (300 MHz; $CDCl_3$): δ 10.13 (t, ^4J = 1.5 Hz, 1H, H^2), 7.28-7.13 (m, 24H, CH_{Ar}), 7.04 (m, 8H, CH_{Ar}), 6.82-6.79 (m, 12H, CH_{Ar}), 5.65 (d, ^4J = 1.5 Hz, 2H, CH_{imid}), 5.05 (s, 4H, CHPh$_2$), 2.21 (s, 6H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$): δ 142.5 (C_{Ar}), 142.0 (C_{Ar}), 141.5 (C_{Ar}), 140.6 (C_{Ar}), 140.3 (CH^2) 130.9 (CH$_{Ar}$), 129.8 (CH$_{Ar}$), 129.3 (CH$_{Ar}$), 128.9 (CH$_{Ar}$), 128.8 (CH$_{Ar}$), 127.2 (CH$_{Ar}$), 127.1 (CH$_{Ar}$), 124.3 (CH$_{imid}$), 51.5 (CHPh$_2$), 22.0 (CH_3).**^{19}F{^{1}H} NMR** (282 MHz; $CDCl_3$): δ -150.50, -150.56. **Anal. Calcd.** for $C_{69}H_{57}BF_4N_2$ (1001.01): C, 82.79; H, 5.74; N, 2.80. Found: C, 82.87; H, 5.59; N, 2.71.

Synthesis of IPr carbene* (**1**): In a glovebox (under Ar atmosphere), NaH (8.48 mmol, 203 mg, 1.50 equiv.) was added to a suspension of **5** (5.65 mmol, 5.65 g, 1.00 equiv.) in anhydrous THF (150 mL). A tip of a spatula of KO^{t}Bu was added. The reaction mixture was stirred overnight at room temperature. The mixture was filtered over a pad of Celite®, and was concentrated *in vacuo*. The resulting solid was then dissolved in the minimum amount of

THF and the product was precipitated by the addition of hexane. It was then collected by filtration to afford **1** (3.19 g, 62%) as a white powder. **^{1}H NMR** (400 MHz; C_6D_6): δ 7.36 (m, 8H, C*H*$_{Ar}$), 7.10-7.08 (m, 8H, C*H*$_{Ar}$), 7.03-6.92 (m, 28H, C*H*$_{Ar}$), 6.03 (s, 4H, C*H*Ph$_2$), 5.78 (s, 2H, C*H*$_{imid}$), 1.85 (s, 6H, C*H*$_3$). **^{13}C{^{1}H} NMR** (101 MHz; C_6D_6): δ 220.02 (*C*$_{carb}$), 145.0 (*C*$_{Ar}$), 143.9 (*C*$_{Ar}$), 142.0 (*C*$_{Ar}$), 138.4 (*C*$_{Ar}$), 138.3 (*C*$_{Ar}$), 130.2 (*C*H$_{Ar}$), 130.0 (*C*H$_{Ar}$), 129.9 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 126.5 (*C*H$_{Ar}$), 126.5 (*C*H$_{Ar}$), 122.6 (*C*H$_{imid}$), 51.5 (*C*HPh$_2$), 21.4 (*C*H$_3$). **Anal. Calcd.** for $C_{69}H_{56}N_2$ (913.20): C, 90.75; H, 6.18; N, 3.07. Found: C, 90.65; H, 6.04; N, 3.14.

Synthesis of [Au(IPr)Cl]* (**C1**): In a glovebox (under Ar atmosphere), a slightly excess of [Au(DMS)Cl] (0.66 mmol, 605 mg, 1.01 equiv.) was added to a solution of **1** (0.66 mmol, 194 mg, 1.00 equiv.) in anhydrous THF (250 mL). Fast colour change to purple was observed. The reaction was stirred for 3 h at room temperature and removed from the glovebox. To the reaction mixture a spatula of charcoal was added and stirred for 20 min. Then, it was filtered over a pad of silica and concentrated *in vacuo*. The resulting solid was then dissolved with a minimum amount of CH_2Cl_2 and precipitated by the addition pentane. The precipitate was collected by filtration to afford **C1** (616 mg, 82%) as a white solid. **^{1}H NMR** (300 MHz; $CDCl_3$): δ 7.19-7.13 (m, 24H, C*H*$_{Ar}$), 7.10-7.07 (m, 8H, C*H*$_{Ar}$), 6.89-6.84 (m, 12H, C*H*$_{Ar}$), 5.81 (s, 2H, C*H*$_{imid}$), 5.26 (s, 4H, C*H*Ph$_2$), 2.23 (s, 6H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz; $CDCl_3$): δ 175.2 (*C*$_{carb}$), 143.0 (*C*$_{Ar}$), 142.3 (*C*$_{Ar}$), 140.9 (*C*$_{Ar}$), 140.2 (*C*$_{Ar}$), 133.8 (*C*$_{Ar}$), 130.3 (*C*H$_{Ar}$), 129.7 (*C*H$_{Ar}$), 129.4 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 128.4 (*C*H$_{Ar}$), 126.7 (*C*H$_{Ar}$), 126.7 (*C*H$_{Ar}$), 123.2 (*C*H$_{imid}$), 51.2 (*C*HPh$_2$), 21.9 (CH$_3$). **Anal. Calcd.** for $C_{69}H_{56}AuClN_2$ (1145.62): C, 72.39; H, 4.93; N, 2.45. Found: C, 72.49; H, 4.84; N, 2.36.

Synthesis of [Au(IPr)NTf$_2$]* (**C2**): To a stirred solution of **C1** (0.17 mmol, 200 mg, 1.00 equiv.) in anhydrous CH_2Cl_2 (2 mL), $AgNTf_2$ (0.18 μmol, 71.0 mg, 1.05 equiv.) was added. Immediate formation of white precipitate was observed. The reaction was stirred for 1 h at room temperature and then filtered over a pad of silica. The solution was then reduced *in vacuo* to a minimum of CH_2Cl_2 and the product was precipitated by the addition of pentane. The precipitate was collected by filtration to afford **C2** (225 mg, 93%) as a white powder. **^{1}H NMR** (400 MHz; $CDCl_3$): δ 7.27-7.20 (m, 12H, C*H*$_{Ar}$), 7.17-7.11 (m, 20H, C*H*$_{Ar}$), 6.83-6.80 (m, 12H, C*H*$_{Ar}$), 5.49 (s, 2H, C*H*$_{imid}$), 5.27 (s, 4H, C*H*Ph$_2$), 2.23 (s, 6H, C*H*$_3$). **^{13}C{^{1}H} NMR** (101 MHz; $CDCl_3$): δ 168.0 (*C*$_{carb}$), 142.9 (*C*$_{Ar}$), 142.4 (*C*$_{Ar}$), 141.1 (*C*$_{Ar}$), 140.6 (*C*$_{Ar}$), 133.2 (*C*$_{Ar}$), 130.3 (*C*H$_{Ar}$), 129.9 (*C*H$_{Ar}$), 129.3 (*C*H$_{Ar}$), 128.7 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 127.02 (*C*H$_{Ar}$), 126.9 (*C*H$_{Ar}$), 123.9 (*C*H$_{imid}$), 120.7 (*C*$_{Ar}$), 117.5 (*C*$_{Ar}$), 51.7 (*C*HPh$_2$), 21.9 (*C*H$_3$). **^{19}F{^{1}H} NMR** (376 MHz; $CDCl_3$): δ -76.4. **Anal. Calcd.** for $C_{71}H_{56}AuF_6N_3O_4S_2$ (1390.01): C, 61.24; H, 4.06; N, 3.02. Found: C, 61.50; H, 3.89; N, 2.87.

Catalyst screening

General Procedure for the Synthesis of Furanone 7: To a solution of 4-hydroxy-4-phenylbut-2-ynoate (**6**) (0.25 mmol, 45 mg) in MeOH (2 mL) the corresponding gold(I)-catalyst (**C2-C9**, 2 mol%) was added and the reaction was stirred at room temperature for 2 h. Solvent was removed *in vacuo*, affording a yellow oil. The reaction conversion was determined by ^{1}H-NMR analysis.

General procedure for the [3,3]-rearrangement of propargylic acetates for the formation of α,β-unsaturated ketones (**9**)*:* In a microwave vial, 1-phenylhept-2-ynyl acetate (**8**) (0.22 mmol, 50 mg) was dissolved in a 10:1 THF/H_2O (2 mL/0.2 mL) mixture and the corresponding gold(I)-catalyst (**C2-C9**, 2 mol%) was added. The reaction mixture was then irradiated in a microwave reactor at 80 ºC for 6 min. The mixture was diluted with pentane, filtered over Celite® and concentrated *in vacuo*, affording a yellow oil. Reaction yields were calculated by ^{1}H NMR using pivalaldehyde as internal standard.

Solvent Screening for the [3,3]-rearrangement of propargylic acetates for the formation of α,β-unsaturated ketones (**9**): In a microwave vial, 1-phenylhept-2-ynyl acetate (**8**) (0.22 mmol, 50 mg) was dissolved in a 10:1 solvent/H_2O (2 mL/0.2 mL) mixture and the corresponding gold(I)-catalyst (**C2-C9**, 2 mol%) was added. The reaction mixture was then irradiated in a microwave reactor at 80 ºC for 6 min. The mixture was diluted with pentane, filtered over Celite® and concentrated *in vacuo*, affording a yellow oil. Reaction yields were calculated by ^{1}H NMR using pivalaldehyde as internal standard.

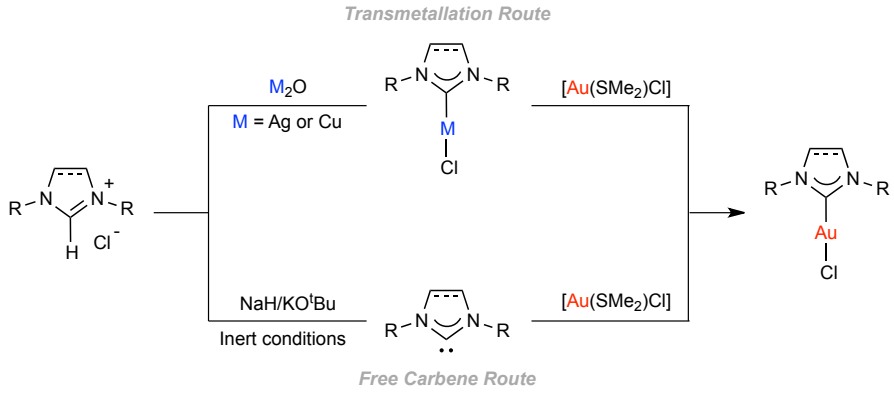
General Procedure for the Synthesis of substituted indenes (**10**): In a microwave vial, **8** (0.22 mmol, 50 mg) was dissolved in DCE (2 mL) and the corresponding gold(I)-catalyst (**C2-C9**, 2 mol%) was added. The reaction mixture was then irradiated in a microwave reactor at 80 ºC for 6 min. The mixture was diluted with pentane, filtered over Celite® and concentrated *in vacuo* affording an oil. Reaction yields were calculated by ^{1}H NMR using pivalaldehyde as internal standard.

General procedure for the synthesis of allylic acetates (**13**): To a solution of **12** (0.28 mmol, 50 mg) in DCE (5 mL), the corresponding gold(I)-catalyst (3 mol%) and AgOTf (2 mol%) were added sequentially and the reaction mixture was then irradiated in a microwave reactor at 80 ºC for 6 min. The conversion was determined by GC.

3. Synthesis of [Au(NHC)X] (X = Cl, Br, I) Complexes

3.1 Introduction

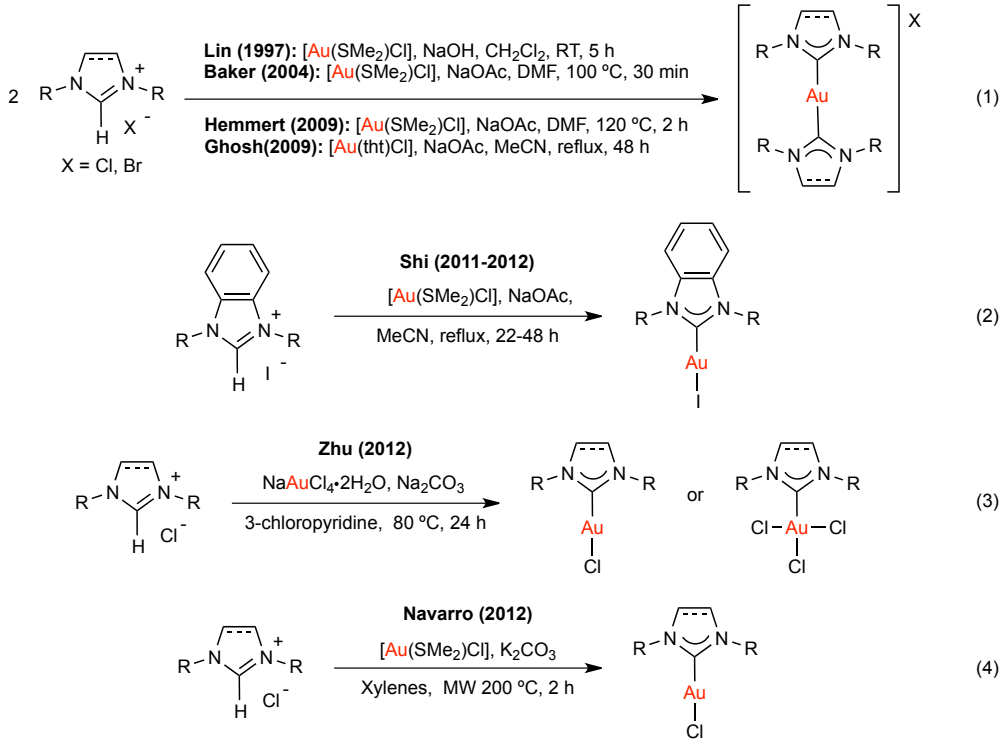
[Au(NHC)X] (X = Cl, Br, I) are key species in gold chemistry. In addition to their ubiquitous use as precatalyst, once activated by a halogen abstractor, they also serve as starting point for the synthesis of several gold species, such as [Au(NHC)(OH)], [Au(NHC)(NTf_2)], [Au(NHC)(MeCN)][BF_4], etc. As seen in Chapter 2 there are two main routes to synthesise [Au(NHC)Cl] complexes: transmetallation from a [M(NHC)Cl] (M = Ag, Cu) precursor,[82a,88,102] or reaction of a suitable gold species, usually [Au(SMe_2)Cl] or [Au(tht)Cl] (tht = tetrahydrothiophene), with a free carbene.[82a] Although both routes have proven to be highly successful for the synthesis of a wide range of Au-NHC complexes, there are several drawbacks intrinsic to each methodology, which could be improved; *e.g.* for the transmetallation route it is necessary to waste 1 equiv. of a metal (Ag or Cu) and for the free carbene route it is mandatory to work under inert conditions and to use relatively strong and expensive bases, such as NaH or KO^{t}Bu (Scheme 1). In addition, none of these routes are of general application for the most common NHC ligands: *e.g.* as seen in Chapter 2, [Au(IPr*)Cl] cannot be synthesised *via* transmetallation from either Ag-NHC or Cu-NHC complexes;[103] and neither [Au(IMes)Cl] nor [Au(SIMes)Cl] can be synthesised *via* the free carbene route.[82a] Therefore, chemists have sought to develop more general, straightforward, economic and efficient synthetic routes towards the synthesis of [Au(NHC)Cl] complexes.



Scheme 1. Common routes for the synthesis of Au-NHC complexes

A literature survey revealed that several research groups have developed one-step routes for the synthesis of Au-NHC species *via* deprotonation of imidazolium salts with weak bases, such as NaOAc and K_2CO_3 (Scheme 2). These procedures can be classified by the type of complexes they afford: a) synthesis of [Au($NHC)_2$][X] (eq. 1, Scheme 2),[104] b) synthesis of [Au(NHC)I] (eq. 2, Scheme 2),[105] and c) synthesis of [Au(NHC)Cl_n] (n = 1 or 3) (eq. 3,

Scheme 3).[106] In 1997, Lin and co-workers reported the first synthesis of $[Au(NHC)_2][Br]$ species using $[Au(SMe_2)Cl]$ and NaOH.[104d] Since then, Baker,[104c] Hemmert,[104a] and Ghosh[104b] have applied some modifications to Lin's strategy (eq. 1, Scheme 2). Shi and co-workers have adapted Ghosh's procedure for the synthesis of [Au(NHC)I] species (eq. 2, Scheme 2), by reducing the equiv. of (benz)imidazolium salt.[105] In addition, Zhu and co-workers have reported the synthesis of either Au^{I}-NHC or Au^{III}-NHC complexes, using 3-chloropyridine as solvent (eq. 3, Scheme 2). This approach has also been successfully used for the synthesis of PEPPSI-Pd precatalysts.[107] Finally, the last example for this kind of strategy has recently been reported by Navarro taking advantage of microwave irradiation to reduce the reaction times (eq. 4, Scheme 2).[106c]



Scheme 2. Synthesis of Au-NHC species *via* deprotonation of imidazolium salts by weak bases.

While the reported protocols for the deprotonation of imidazolium salts with weak bases offer a direct and straightforward approach to the synthesis of Au-NHC species, they present several drawbacks: a) narrow scope, b) use of relatively high temperatures (80-200 ºC), c) long reaction times (2-48 h), and d) the use of environmentally unfriendly solvents, such as xylenes, 3-chloropyridine and dimethylformamide (DMF).[108] With the increased use of Au-NHC catalysts in organic synthesis, there is always a need for more efficient ways to synthesise them. Therefore, the development of improved, scalable, economical and general procedures for the synthesis of a wide range of [Au(NHC)Cl] species is highly desirable. In

this Chapter we present our findings regarding the synthesis of [Au(NHC)(X)] (X = Cl, Br, I) complexes by reacting the corresponding imidazolium salts with [Au(SMe_2)Cl] and a weak base.

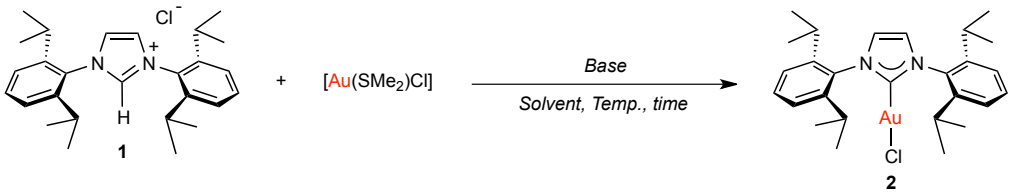
3.2 Results and discussion

3.2.1 *Optimisation of the Reaction Conditions*

Since IPr•HCl (**1**) is one the most common imidazolium salts, it is commercially available, and leads to typically the most reactive catalysts, we decided to use it as our standard substrate during the optimisation studies. We began our investigations by using the reaction conditions reported by Shi and co-workers,[109] *i.e.* 2 equiv. of NaOAc, 1 equiv. of [Au(SMe_2)Cl], and dry acetonitrile under a nitrogen atmosphere. Gratifyingly, after 24 h at room temperature, we observed an encouraging 70% conversion to [Au(IPr)Cl] (**2**) by ^{1}H NMR. Subsequent variations on this protocol, such as performing the reactions under air or using non-dry solvents, did not have a detrimental impact on the observed conversions. Therefore, further solvent and base screenings were carried out under these user-friendly conditions and the conversions examined by ^{1}H NMR spectroscopy (Table 1). The reaction also worked using [Au(tht)Cl] as the gold source, but for practical reasons we decided to carry out our studies using [Au(SMe_2)Cl].

First we examined several bases using acetonitrile as solvent at room temperature (Entries 1-5, Table 1). The best conversions were obtained using K_2CO_3 (85%) and triethylamine (89%) (Entries 2 and 5, Table 1). Regarding the solvent, the best conversions at room temperature were obtained in acetone, where **2** was obtained in 99% conversion after 24 h (Entry 6, Table 1). By increasing the temperature to 60 ºC we were able to reduce the necessary equiv. of K_2CO_3 by half, and the reaction time to 1 h (Entry 10, Table 1). We were very pleased to observe that performing the reaction under inert conditions had no impact on the conversions to **2** (Entries 11 and 12, Table 1). Changing K_2CO_3 for triethylamine or pyridine did not improve the transformation (Entries 16 and 17, Table 1). Therefore, we selected 1 equiv. of K_2CO_3 in acetone at 60 ºC as our optimised reaction conditions. With this set of conditions in hand, **2** was isolated in an excellent 97% yield and elemental analysis was performed on this sample to confirm the purity of the material produced by our methodology.

Table 1. Screening of the reaction conditions[a]



Entry	Base	Equiv. of base	Solvent	T (ºC)	T (h)	Conversion (%)[b]
1	NaOAc	2	CH_3CN	25	24	70
2	K_2CO_3	2	CH_3CN	25	24	85
3	$NaHCO_3$	2	CH_3CN	25	24	25
4	Na_2CO_3	2	CH_3CN	25	24	63
5	NEt_3	2	CH_3CN	25	24	89
6	K_2CO_3	2	Acetone	25	24	>99
7	K_2CO_3	2	^{i}PrOH	25	24	87
8	K_2CO_3	2	CH_3CN	40	24	>99
9	K_2CO_3	2	Acetone	40	24	>99
10	**K_2CO_3**	**1**	**Acetone**	**60**	**1**	**>99 (97)**
11[c]	K_2CO_3	1	Acetone	60	1	>99
12[d]	K_2CO_3	1	Acetone	60	1	>99
13	K_2CO_3	1	THF	60	1	23
14	K_2CO_3	1	Me-THF	60	1	25
15	K_2CO_3	1	^{i}PrOH	60	1	90
16	NEt_3	1	Acetone	60	1	80
17	Pyridine	1	Acetone	60	24	0

[a] Reaction conditions: **1** (0.235 mmol), [Au(SMe$_2$)Cl] (0.235 mmol), base (1-2 equiv), solvent (1 mL). Unless otherwise noted, the reactions were carried out under air using technical grade solvents. [b] Conversion given by ^{1}H NMR analysis of an aliquot of the reaction mixture. Isolated yield in parenthesis. c) Dry acetone was used. d) The reaction was conducted under argon, using dry acetone

3.2.2 *Scope*

Next, we proceeded to examine the generality of our procedure (Table 2). We decided to test our new synthetic protocol on the imidazolium and imidazolidinium salts shown in Figure 1. We started our studies using unsaturated imidazolium salts bearing *N*-aryl substituents (Entries 1-5, Table 10). The reaction proved to be highly efficient and the desired complexes were obtained in good to excellent yields (76-97%). 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] (**2**) and [Au(IMes)Cl] complexes. **2** was obtained in 97% yield (Entry 1, Table 2), while 76% yield is achieved following the free carbene route (*ca*. 60% overall yield, taking into account that the free carbene must be isolated).[82a] For [Au(IMes)Cl], the yield has been improved from 63% (obtained by transmetallation) to 79% (Entry 2, Table 2).[82a] Noteworthy is the isolation of challenging gold complexes such as [Au(IPr*)Cl], which cannot be prepared by transmetallation, in a 76% yield after 4 h (Entry 3, Table 2).[103] Next, we decided to explore the applicability of our methodology to *N*-alkyl substituted imidazolium salts. Gratifyingly, good yields were

obtained (60-80%) (Entries 6-9, Table 2). Nevertheless, the reactions for ICy•HCl, IDD•HCl and I^{t}Bu•HCl did not reach completion and decomposition of the product was observed after long reaction times, thus the reactions were stopped after 2-3 h in order to maximise the yields (Entries 7-9, Table 2).

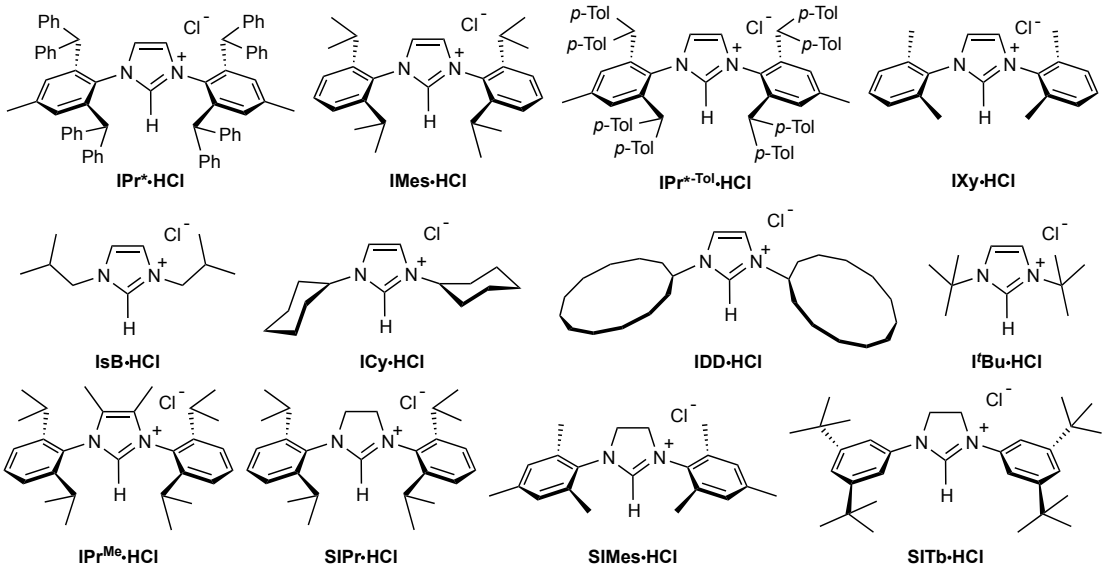
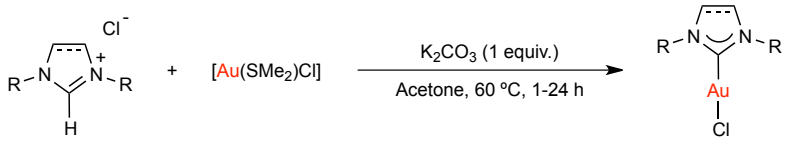


Figure 1. Imidazolium and imidazolidinium salts used during this study

Table 2. 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

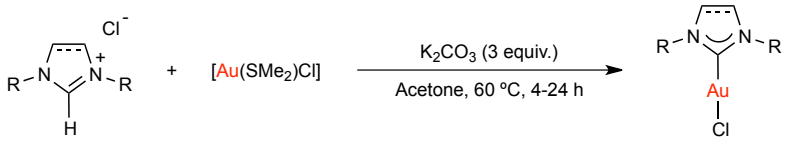
[a] Reaction conditions: NHC•HCl (100 mg), [Au(SMe$_2$)Cl] (1 equiv.), K$_2$CO$_3$ (1 equiv.), acetone (1 mL), 60 ºC. [b] K$_2$CO$_3$ (2 equiv.).

The substitution on the imidazolium backbone had a dramatic effect on the reaction and only 53% yield of the desired Au-complex was obtained after 4 h using IPr^{Me}•HCl. However,

if the amount of base is increased to 2 equiv. the yield can be improved to 78% (Entry 10, Table 2). 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%.[110] Interestingly, longer reaction times are required to reach full conversion for saturated NHC ligands (Entries 11-13, Table 2). The desired gold complexes were obtained in good yields (68-82%) after 24 h (Entries 11-13, Table 2). All complexes were characterised by ^{1}H and ^{13}C{^{1}H} NMR spectroscopies and data for the reported complexes matched literature spectra.[103,110-111]

Interested by the scalability of this new synthetic protocol, the preparation of several [Au(NHC)Cl] species was carried out on a larger scale (Table 3). Although the reactions worked well using 1 equiv. of K_2CO_3, the addition of extra K_2CO_3 significantly reduced the reaction times, thus the large scale reactions were carried out using 3 equiv. of K_2CO_3. Gratifyingly, all the reactions proceeded without problems and the desired [Au(NHC)Cl] complexes were obtained in good to excellent yields (Table 3).

Table 3. Large scale reactions[a]

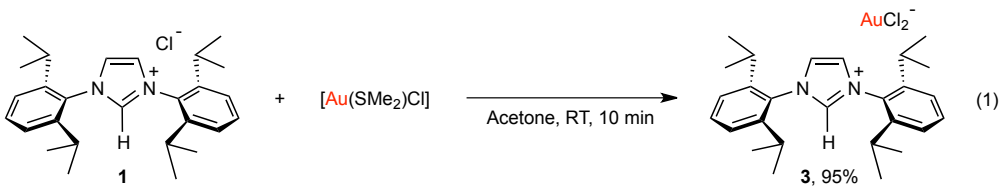


Entry	NHC•HCl	[Au(SMe$_2$)Cl] (g)	Time (h)	Yield (g)
1	IPr•HCl	15.0	5	29.8 (94%)
2	IMes•HCl	20.0	5	31.6 (87%)
3	ICy•HCl	3.29	4	3.91 (75%)
4	IPr^{Me}•HCl	1.22	4	2.11 (77%)
5	SIMes•HCl	2.58	24	3.74 (79%)

[a] Reaction conditions: acetone, 60 °C, 1 equiv. of NHC•HCl, 1 equiv. of [Au(SMe$_2$)Cl], 3 equiv. of K_2CO_3.

3.2.3 *Mechanistic Investigations*

In order to gain a deeper understanding of the reaction mechanism, IPr•HCl (**1**) was reacted with [Au(SMe$_2$)Cl] in the absence of K_2CO_3. After 10 min at room temperature complete conversion to a new species could be observed by ^{1}H NMR spectroscopy (eq. 1).



This compound was isolated as a white solid in 95% yield and unambiguously characterised by ^{1}H, ^{13}C{^{1}H} NMR spectroscopy, 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)º (Figure 2). Interestingly, a 2.11 ppm upfield shift can be observed in the ^{1}H NMR of **3** for the signal corresponding to the NC*H*N proton, relative to the starting material IPr•HCl (8.89 *vs*. 11.0 ppm).

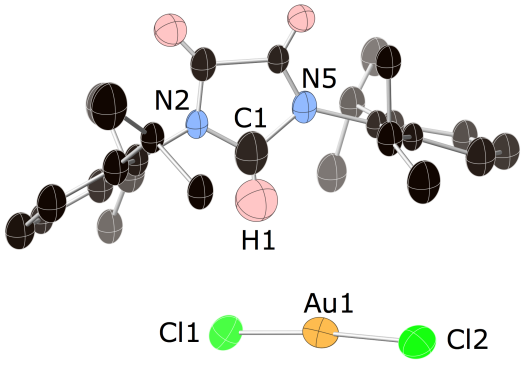
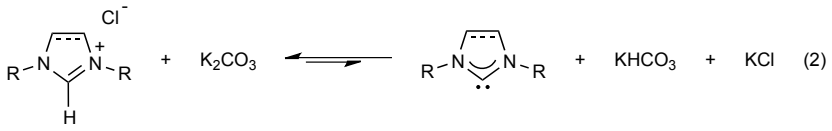
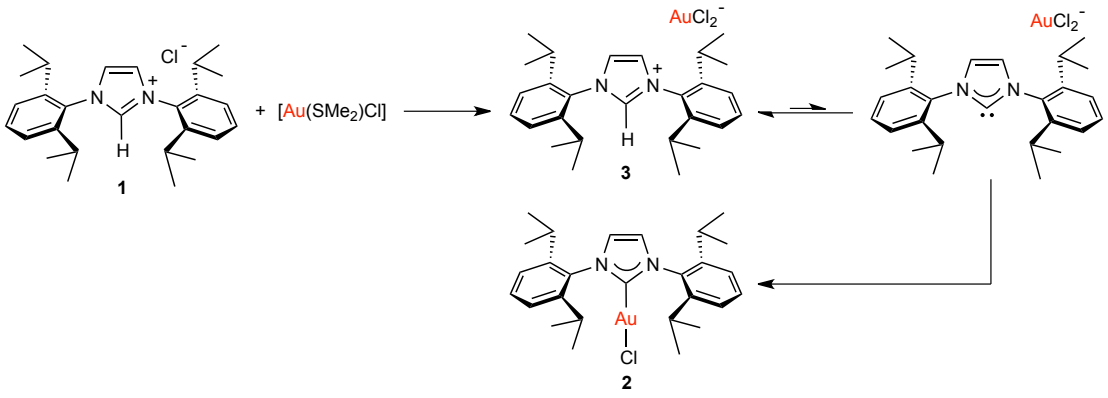


Figure 2. Thermal ellipsoid representation of **3**. Most H atoms were omitted for clarity.

Subsequent treatment of **3** with 1 equiv. of K_2CO_3 afforded the desired complex [Au(IPr)Cl] quantitatively. This result supports the hypothesis that **3** is an intermediate species in this process. Theoretically, it should not be possible for a weak base such as K_2CO_3 to deprotonate an imidazolium salt to form appreciable quantities of the corresponding free carbene, as there is a huge difference in pK_a between the two species (p$K_{a\,(water)}$ NHC salts = 19.0-25.4[112] *vs*. p$K_{a\,(water)}$ K_2CO_3 = 6.37-10.25). However, as the pK_a reflects the equilibrium between an acid and its conjugate base, the interaction between an imidazolium salt and K_2CO_3 can also be seen as an equilibrium strongly displaced toward the former (eq. 2). The same applies to the interaction between intermediate **3** and K_2CO_3, as the O'Donoghue group has reported that the counterion has little effect on the pK_a of imidazolium salts.[112]

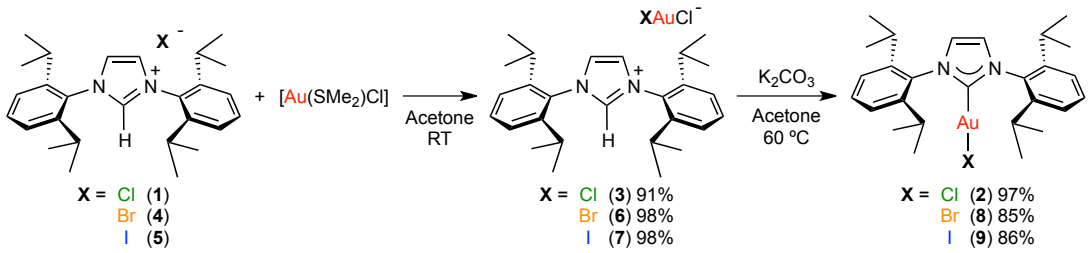


Based on these studies, we proposed the following mechanism (Scheme 3): the first step of the reaction would be the formation of intermediate **3**, which in the presence of K_2CO_3 would be in equilibrium with the free carbene. Although this equilibrium is strongly displaced towards **3**, the small amount of free carbene present in solution would immediately react with Au to form the final product **2**. Thus, the driving force of the reaction would be the formation of the [Au(NHC)Cl] species.



Scheme 3. Proposed reaction mechanism

Interested by the nature of intermediate **3**, *i.e.* an imidazolium 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 the final gold complex would be once these species were treated with base. Therefore, $[Au(SMe_2)Cl]$ was reacted with IPr•HBr (**4**) and IPr•HI (**5**). Gratifyingly, after 10 min. quantitative conversions to [IPrH][AuClBr] (**6**) and [IPrH][AuClI] (**7**) were observed. Subsequent treatment of these species with 1 equiv. of K_2CO_3 led to the formation of a single Au-NHC species in each case, [Au(IPr)Br] (**8**) and [Au(IPr)I] (**9**) respectively (Scheme 4). Interestingly, formation of the chloride derivative **2** was never observed during these reactions. Moreover, the nature of compounds **6**-**9** was further confirmed by ^1H and $^{13}C\{^1H\}$ NMR spectroscopy as well as elemental analyses.



Scheme 4. Selective formation of [Au(NHC)X] (X = Cl, Br, I)

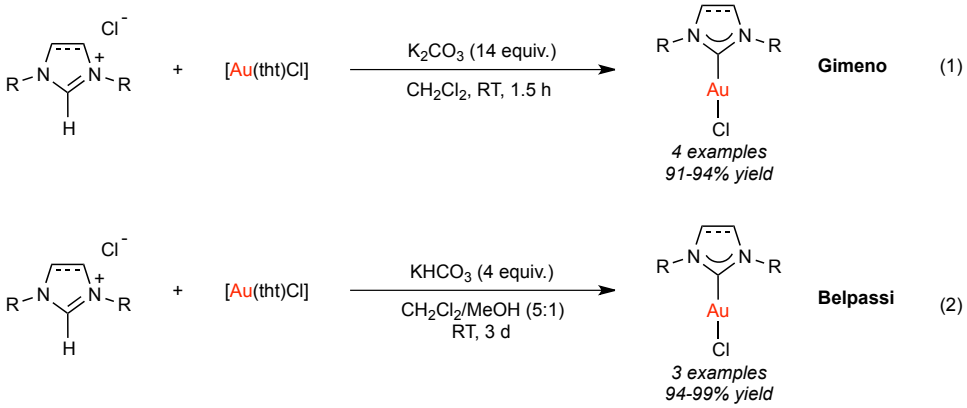
The selective formation of bromide (**8**) and iodide (**9**) derivatives, over the chloride species (**2**), can be rationalised based on the halide *trans* effect on the $[X\text{-}Au\text{-}Cl]^-$ (X = Br, I) unit of intermediates **6** and **7**. The halide exerting a higher *trans* effect (I >> Br > Cl >>F)[113] would labilise the bond *trans* to it, thus staying coordinated to the gold centre in the final complex. Moreover, the formation of KCl is more favourable than KBr or KI. This would explain why we observed formation of **8** and **9** rather than **2**, when using NHC•HX (X = Br, I) salts. This hypothesis would also explain the formation of [Au(NHC)I] complexes observed by Shi when starting from NHC•HI salts (eq. 2, Scheme 2).

Therefore, our new synthetic protocol can be tuned to synthesise [Au(NHC)X] (X = Br, I) in one-pot. These type of complexes are usually synthesised from [Au(NHC)Cl] species by salt metathesis with, for example, LiX (Br, I); thus our new procedure offers a more straightforward pathway for the synthesis of this kind of complexes.

3.3 Conclusion

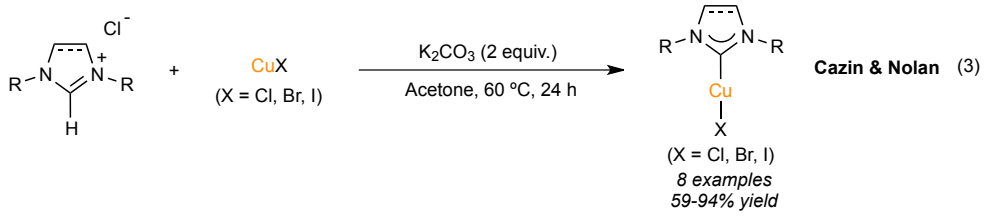
In summary, we have developed a straightforward, economical and efficient synthetic route for the synthesis of [Au(NHC)Cl] complexes. This new protocol is based on the deprotonation of NHC•HCl salts by K_2CO_3 in the presence of [Au(SMe_2)Cl], and it works under air and using technical grade acetone. Moreover, it is applicable to a wide range of NHC•HCl salts, such as un/saturated, as well as *N*-aryl and *N*-alkyl substituted. In addition, our synthetic protocol is highly versatile; by selecting the starting salt, either NHC•HCl, NHC•HBr or NHC•HI, we can selectively access the corresponding [Au(NHC)X] (X = Cl, Br or I) complexes. This new procedure is also highly scalable. Slight variations to the reported procedure, such as the amount of base, have allowed our group to synthesise 200 g of [Au(IPr)Cl] in 96% yield after 2 h.

After the publication of our investigations, several groups have reported similar protocols for the synthesis of [Au(NHC)Cl] complexes. In concomitance with the publication of our investigations, Gimeno and co-workers independently reported a very similar procedure for the synthesis of [Au(NHC)Cl] species (eq. 1, Scheme 5).[114] They managed to synthesise a series of [Au(NHC)Cl] complexes at room temperature within 1.5 h, by using a large excess of K_2CO_3 (14 equiv.) in CH_2Cl_2. They also proposed the formation of [IPrH][$AuCl_2$] as a reaction intermediate. Belpassi and co-workers have recently reported a variation of this protocol where they dissolved the NHC•HCl salt in a 5:1 mixture of CH_2Cl_2/MeOH and reacted it with 4 equiv. of $KHCO_3$ at room temperature for 3 days, to obtain the desired [Au(NHC)Cl] species in high yields (94-99%) (eq. 2, Scheme 5).[115]



Scheme 5. Similar protocols for the synthesis of [Au(NHC)Cl] species

In addition, our group, in collaboration with Cazin and co-workers, has recently reported a variation of our synthetic protocol for the synthesis of [Cu(NHC)X] (X = Cl, Br, I) complexes (eq. 3).[116]



3.4 Experimental Section

All reactions were carried under air and technical grade solvent were used unless otherwise stated. K_2CO_3, Na_2CO_3, $NaHCO_3$, NaOAc, pyridine and NEt_3 were used as received without further purification. ^1H, and $^{13}C\{^1H\}$ NMR spectra were recorded on a Bruker-400 MHz or 300 MHz spectrometer at ambient temperature in CD_2Cl_2. Chemical shifts (expressed in parts per million) are referenced to residual solvent peaks. Elemental analyses were performed at London Metropolitan University 166-220 Holloway Road, London, N7 8DB. CCDC 830311 (**3**) contains the supplementary crystallographic data for this contribution. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre (CCDC) *via* http://www.ccdc.cam.ac.uk/data_request/cif.

General procedure for the synthesis of [Au(NHC)Cl] complexes:

- *Small scale:* A vial was charged, under air, with the corresponding NHC•HCl (100 mg, 1 equiv), [Au(SMe_2)Cl] (1 equiv) and K_2CO_3 (1 equiv). The resulting mixture was suspended in acetone (1.0 mL) and stirred for 1-24 h at 60ºC. After this time the solvent was removed *in vacuo* and dichloromethane was added. The mixture was filtered through silica. The pad of silica was washed with dichloromethane (3 x 1 mL). The solvent was concentrated and pentane (3 mL) was added, affording a white solid that was washed with further portions of pentane (3 x 1 mL) and dried under vacuum.
- *Large scale:* A round bottom flask equipped with a condenser was charged under air with the corresponding NHC•HCl (1 equiv), [Au(SMe_2)Cl] (1 equiv) and K_2CO_3 (3 equiv). The resulting mixture was dissolved in acetone and stirred for 3-24 h at 60ºC. The same work up was carried out affording the corresponding complexes as white solids in high yields.

Preparation of [Au(IPr)Cl]: Following the small scale general procedure, a mixture of IPr•HCl (100 mg, 0.235 mmol), [Au(SMe_2)Cl] (69.3 mg, 0.235 mmol) and K_2CO_3 (32.5 mg,

0.235 mmol) in acetone (1.0 mL) was stirred for 1 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 97% yield (143 mg, 0.228 mmol). The ^{1}H and ^{13}C{^{1}H} NMR spectra matched those reported in the literature.[117] **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.57 (t, *J* = 7.8, 2H, C*H*$_{Ar}$), 7.35 (d, *J* = 7.8, 4H, C*H*$_{Ar}$), 7.24 (s, 2H, C*H*$_{imid}$), 2.56 (sept, *J* = 6.9, 4H, C*H*$_{iPr}$), 1.34 (d, *J* = 6.9, 12H, C*H*$_3$), 1.23 (d, *J* = 6.9, 12H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2, 293 K): δ 175.7 (*C*$_{carb}$), 146.4 (*C*$_{Ar}$), 134.6 (*C*$_{Ar}$), 131.2 (*C*H$_{Ar}$), 124.8 (*C*H$_{Ar}$), 123.9 (*C*H$_{imid}$), 29.4 (*C*H$_{iPr}$), 24.7 (*C*H$_3$), 24.3 (*C*H$_3$). **Anal. Calcd.** for $C_{27}H_{36}AuClN_2$ (620.22): C, 52.22; N, 4.51; H, 5.84. Found: C, 52.33; N, 4.60; H, 5.91.

Preparation of [Au(IMes)Cl]: Following the small scale general procedure, a mixture of IMes•HCl (100 mg, 0.294 mmol), [Au(SMe$_2$)Cl] (86.6 mg, 0.294 mmol) and K_2CO_3 (40.6 mg, 0.294 mmol) in acetone (1 mL) was stirred for 4 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 79% yield (124 mg, 0.232 mmol). The ^{1}H and ^{13}C{^{1}H} NMR spectra matched those reported in the literature.[82a] **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.16 (s, 2H, C*H*$_{imid}$), 7.07 (s, 4H, C*H*$_{Ar}$), 2.38 (s, 6H, C*H*$_3$), 2.13 (s, 12H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 173.5 (*C*$_{carb}$), 140.5 (*C*$_{Ar}$), 135.4 (*C*$_{Ar}$), 135.3 (*C*$_{Ar}$), 129.9 (*C*H$_{Ar}$), 123.0 (*C*H$_{imid}$), 21.5 (*C*H$_3$), 18.1 (*C*H$_3$).

Preparation of [Au(IPr)Cl]:* Following the small scale general procedure, a mixture of IPr*•HCl (100 mg, 0.105 mmol), [Au(SMe$_2$)Cl] (31.0 mg, 0.105 mmol) and K_2CO_3 (13.5 mg, 0.105 mmol) in acetone (1.0 mL) was stirred for 4 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 76% yield (91.4 mg, 0.080 mmol). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ 7.17 (m, 24H, C*H*$_{Ar}$), 7.12-7.10 (m, 8H, C*H*$_{Ar}$), 6.93 (s, 4H, C*H*$_{Ar}$), 6.89-6.87 (m, 8H, C*H*$_{Ar}$), 5.85 (s, 2H, C*H*$_{imid}$), 5.26 (s, 4H, C*H*Ph$_2$), 2.25 (s, 6H, C*H*$_3$).**^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ 175.6 (*C*$_{carb}$), 143.1 (*C*$_{Ar}$), 142.9 (*C*$_{Ar}$), 141.3 (*C*$_{Ar}$), 140.8 (*C*$_{Ar}$), 134.1 (*C*$_{Ar}$), 130.6 (*C*H$_{Ar}$), 130.1 (*C*H$_{Ar}$), 129.7 (*C*H$_{Ar}$), 128.8 (*C*H$_{Ar}$), 127.1 (*C*H$_{Ar}$), 127.0 (*C*H$_{Ar}$), 123.6 (*C*H$_{imid}$), 51.6 (*C*HPh$_2$), 21.9 (C*H*$_3$).

Preparation of [Au(IPr^{*-Tol})Cl]:* Following the small scale general procedure a mixture of IPr^{*-Tol}•HCl (100 mg, 0.094mmol), [Au(SMe$_2$)Cl] (27.7 mg, 0.094 mmol) and K_2CO_3 (13.0 mg, 0.094 mmol) in acetone (1 mL) was stirred for 2 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 88% yield (104 mg, 0.083 mmol). ^{1}H NMR (300 MHz; CD_2Cl_2): δ 7.00 (s, 14H, C*H*$_{Tol}$), 6.97 (d, *J* = 7.8 Hz, 8H, C*H*$_{Tol}$), 6.92 (s, 4H, C*H*$_{Ar}$), 6.74 (d, *J* = 8.0 Hz, 8H, C*H*$_{Tol}$), 5.88 (s, 2H, C*H*$_{imid}$), 5.18 (s, 4H, C*H*(Tol)$_2$), 2.28 (s, 24H, C*H*$_{3\ Tol}$), 2.25 (s, 6H, C*H*$_{3\ Ar}$). **^{13}C{^{1}H} NMR** (75 MHz; CD_2Cl_2): δ 175.4 (*C*$_{carb}$), 141.6 (*C*$_{Ar}$), 140.5 (*C*$_{Ar}$), 140.3 (*C*$_{Tol}$), 140.2 (*C*$_{Tol}$), 136.65 (*C*$_{Tol}$), 136.48 (*C*$_{Tol}$), 134.1 (*C*$_{Ar}$), 130.3 (*C*H$_{Ar}$),

129.8 (*C*H$_{Tol}$), 129.49 (*C*H$_{Tol}$), 129.37 (*C*H$_{Tol}$), 123.6 (*C*H$_{imid}$), 50.8 (*C*H(Tol)$_2$), 21.9 (C*H*$_{3\ Ar}$), 21.12 (C*H*$_{3\ Tol}$), 21.08 (C*H*$_{3\ Tol}$). **Anal. Calcd.** for $C_{77}H_{72}AuClN_2$ (1257.83): C, 73.53; N, 2.23; H, 5.77. Found: C, 73.34; N, 2.34; H, 5.64.

Preparation of [Au(IXy)Cl]: Following the small scale general procedure, a mixture of IXy•HCl (100 mg, 0.320 mmol), [Au(SMe$_2$)Cl] (94.4 mg, 0.320 mmol) and K_2CO_3 (44.3 mg, 0.320 mmol) in acetone (1 mL) was stirred for 1 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 97% yield (156 mg, 0.310 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.39 (m, 2H, C*H*$_{Ar}$), 7.27 (d, *J* = 7.6, 4H, C*H*$_{Ar}$), 7.20 (s, 2H, C*H*$_{imid}$), 2.18 (s,12H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 173.5 (*C*$_{carb}$), 137.8 (*C*$_{Ar}$), 135.9 (*C*$_{Ar}$), 130.4 (*C*H$_{Ar}$), 129.3 (*C*H$_{Ar}$), 122.9 (*C*H$_{imid}$), 18.2 (*C*H$_3$). **Anal. Calcd.** for $C_{19}H_{20}AuClN_2$ (508.79): C, 44.85; N, 5.51; H, 3.96. Found: C, 44.75; N, 5.47; H, 3.87.

Preparation of [Au(IsB)Cl]: Following the small scale general procedure, a mixture of IsB•HCl (100 mg, 0.461 mmol), [Au(SMe$_2$)Cl] (135.9 mg, 0.461 mmol) and K_2CO_3 (63.8 mg, 0.461 mmol) in acetone (1 mL) was stirred for 1 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 88% yield (168 mg, 0.406 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 6.95 (s, 2H, C*H*$_{imid}$), 3.97 (d, *J* = 7.5 Hz, 4H, C*H*$_2$), 2.23 (m, 2H, C*H*), 0.95 (d, *J* = 6.7 Hz, 12H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 171.2 (*C*$_{carb}$), 121.3 (*C*H$_{imid}$), 59.1 (*C*H$_2$), 30.7 (*C*H), 20.1 (*C*H$_3$). **Anal. Calcd.** for $C_{11}H_{20}AuClN_2$ (412.71): C, 32.01; N, 6.79; H, 4.88. Found: C, 31.97; N, 6.79; H, 4.92.

Preparation of [Au(ICy)Cl]: Following the small scale general procedure, a mixture of ICy•HCl (100 mg, 0.371 mmol), [Au(SMe$_2$)Cl] (109.5 mg, 0.371 mmol) and K_2CO_3 (51.4 mg, 0.371 mmol) in acetone (1.0 mL) was stirred for 2 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 75% yield (129.3 mg, 0.278 mmol). The ^{1}H and ^{13}C{^{1}H} NMR matched those reported in the literature.[82a] **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.00 (s, 2H, C*H*$_{imid}$), 4.56 (tt, *J* = 11.9, 3.9 Hz, 2H, C*H*), 2.08 (dd, *J* = 12.7, 2.0 Hz, 4H, C*H*$_2$), 1.89-1.86 (m, 4H, C*H*$_2$), 1.76-1.73 (m, 2H, C*H*$_2$), 1.61 (qd, $J_{H\text{-}H}$= 12.4, 3.4 Hz, 4H, C*H*$_2$), 1.47 (qt, *J* = 13.1, 3.2 Hz, 4H, C*H*$_2$), 1.22 (qt, *J* = 12.9, 3.7 Hz, 2H, C*H*$_2$). **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ 168.7 (*C*$_{carb}$), 117.6 (*C*H$_{imid}$), 61.4 (*C*H), 34.4 (*C*H$_2$), 25.8 (*C*H$_2$), 25.5 (*C*H$_2$).

Preparation of [Au(IDD)Cl]: Following the small scale general procedure, a mixture of IDD•HCl (100 mg, 0.228 mmol), [Au(SMe$_2$)Cl] (67.2 mg, 0.228 mmol) and K_2CO_3 (31.6 mg, 0.228 mmol) in acetone (1.0 mL) was stirred for 3 h at 60 ºC. After the workup, the desired

complex was obtained as a white solid in 70% yield (101 mg, 0.159 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 6.97 (s, 2H, CH_{imid}), 4.87 (quintet, J = 6.5 Hz, 2H, C$H_{cyclododecanyl}$), 2.06-1.95 (m, 4H, CH_2), 1.66-1.48 (m, 10H, CH_2), 1.48-1.28 (m, 30H, CH_2). **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ 170.0 (C_{carb}), 118.1 (CH$_{imid}$), 58.1 (CH$_{cyclododecanyl}$), 31.5 (CH$_2$), 24.2 (CH$_2$), 23.9 (CH$_2$), 23.7 (CH$_2$), 23.4 (CH$_2$), 22.0 (CH$_2$).

Preparation of [Au(I^{t}Bu)Cl]: Following the small scale general procedure, a mixture of I^{t}Bu•HCl (100 mg, 0.461 mmol), [Au(SMe$_2$)Cl] (135.8 mg, 0.461 mmol) and K_2CO_3 (63.8 mg, 0.461 mmol) in acetone (1.0 mL) was stirred for 2 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 60% yield (114 mg, 0.276 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.12 (s, 2H, CH_{imid}), 1.86 (s, 18H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 168.4 (C_{carb}), 116.8 (CH$_{imid}$), 59.22 ($C_{t\text{Bu}}$), 31.9 (CH$_3$).

Preparation of [Au(IPr^{Me})Cl]: Following the small scale general procedure, a mixture of IPr^{Me}•HCl (100 mg, 0.221 mmol), [Au(SMe$_2$)Cl] (65.0 mg, 0.221 mmol) and K_2CO_3 (30.5 mg, 0.221 mmol) in acetone (1.0 mL) was stirred for 5 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 53% yield (76 mg, 0.117 mmol). When the reaction was run using 2 equiv of K_2CO_3 (61.0 mg, 0.442 mmol) the isolated yield was 78%. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ 7.57 (t, J = 7.8 Hz, 2H, CH_{Ar}), 7.36 (d, J = 7.8 Hz, 4H, CH_{Ar}), 2.47 (sept, J= 6.9 Hz, 4H, C$H_{i\text{Pr}}$), 1.95 (s, 6H, CH_3), 1.34 (d, J = 6.9 Hz, 12H, C$H_{3\ i\text{Pr}}$), 1.25 (d, J = 6.9 Hz, 12H, C$H_{3\ i\text{Pr}}$). **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ 171.3 (C_{carb}), 146.4 (C_{Ar}), 132.9 (C_{Ar}), 130.9 (CH$_{Ar}$), 126.8 ($C_{2\text{-imid}}$), 124.7 (CH$_{Ar}$), 29.0 (CH$_{i\text{Pr}}$), 25.2 (CH$_{3\ i\text{Pr}}$), 23.5 (CH$_{3\ i\text{Pr}}$), 9.9 (CH$_3$).

Preparation of [Au(SIPr)Cl]: Following the small scale general procedure, a mixture of SIPr•HCl (100 mg, 0.234 mmol), [Au(SMe$_2$)Cl] (69.0 mg, 0.234 mmol) and K_2CO_3 (32.9 mg, 0.234 mmol) in acetone (1.0 mL) was stirred for 24 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 78% yield (114 mg, 0.182 mmol). The ^{1}H and ^{13}C{^{1}H} NMR matched those reported in the literature.[82a] **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.48 (t, J = 7.7, 2H, CH_{Ar}), 7.29 (d, J = 7.7, 4H, CH_{Ar}), 4.06 (s, 4H, C$H_{2\text{-imid}}$), 3.07 (sept, J = 6.9 Hz, 4H, C$H_{i\text{Pr}}$), 1.40 (d, J= 6.9, 12H, CH_3), 1.34 (d, $J_{H\text{-}H}$ = 6.9, 12H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 196.4 (C_{carb}), 147.3 (C_{Ar}), 134.7 (C_{Ar}), 130.5 (CH$_{Ar}$), 125.2 (CH$_{Ar}$), 54.1 (CH$_{2\text{-imid}}$), 29.5 (CH$_{i\text{Pr}}$), 25.4 (CH$_3$), 24.4 (CH$_3$).

Preparation of [Au(SIMes)Cl]: Following the small scale general procedure, a mixture of SIMes•HCl (100 mg, 0.292mmol), [Au(SMe$_2$)Cl] (86.1 mg, 0.292 mmol) and K_2CO_3 (40.4

mg, 0.292 mmol) in acetone (1.0 mL) was stirred for 24h at 60ºC. After the workup, the desired complex was obtained as a white solid in 82% yield (129 mg, 0.239 mmol). The ^{1}H and $^{13}C\{^{1}H\}$ NMR matched those reported in the literature.[82a] **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.02 (s, 4H, CH_{Ar}), 4.00 (s, 4H, C$H_{2\text{-imid}}$), 2.33 (s, 18H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 195.1 (C_{carb}), 139.5 (C_{Ar}), 136.2 (C_{Ar}), 135.1 (C_{Ar}), 130.0 (CH_{Ar}), 51.1 ($CH_{2\text{-imid}}$), 21.3 (CH_3), 18.2 (CH_3).

Preparation of [Au(SITb)Cl]: Following the small scale general procedure, a mixture of SITb•HCl (100 mg, 0.207 mmol), [Au(SMe_2)Cl] (61.1 mg, 0.207 mmol) and K_2CO_3 (28.7 mg, 0.207 mmol) in acetone (1.0 mL) was stirred for 24 h at 60ºC. After the workup, the desired complex was obtained as a white solid in 68% yield (96 mg, 0.141 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.56 (d, J = 1.7, 4H, CH_{Ar}), 7.41 (t, J = 1.7, 2H, CH_{Ar}), 4.31 (s, 4H, CH_{imid}), 1.37 (s, 36H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 190.5 (C_{carb}), 152.7 (C_{Ar}), 140.8 (C_{Ar}), 121.9 (CH_{Ar}), 118.0 (CH_{Ar}), 51.7 ($CH_{2\text{-imid}}$), 35.6 ($C_{t\text{Bu}}$), 31.6 (CH_3). **Anal. Calcd.** for $C_{31}H_{16}AuClN_2$ (677.11): C, 54.82; N, 4.12; H, 6.83. Found: C, 54.75; N, 4.23; H, 6.88.

*Preparation of [IPrH][AuCl$_2$] (**3**):* A vial was charged with IPr•HCl (100 mg, 0.235 mmol), and [Au(SMe_2)Cl] (69.3 mg, 0.235 mmol). The resulting mixture was dissolved in acetone (1.0 mL) and stirred for 10 min at room temperature. After this time the mixture was filtered through Celite®. The solvent was concentrated and pentane (3 mL) was added, affording a white solid which was washed with further portions of pentane (3 x 1 mL) and dried under vacuum to afford **3** as a white solid in 91% yield (141 mg, 0.214 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 8.89 (t, J = 1.5, 1H, CH_{NCN}), 7.79 (d, J = 1.5, 2H, CH_{imid}), 7.66 (t, J = 7.9, 2H, CH_{Ar}), 7.42 (d, J = 7.9, 4H, CH_{Ar}), 2.41 (sept, J = 6.9, 4H, C$H_{i\text{Pr}}$), 1.31 (d, J = 6.9, 12H, CH_3), 1.24 (d, J = 6.9, 12H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 145.4 (C_{Ar}), 137.7 (CH_{NCN}), 133.2 (C_{Ar}), 129.9 (C_{Ar}), 126.7 (CH_{imid}), 125.6 (CH_{Ar}), 29.8 ($CH_{i\text{Pr}}$), 25.0 (CH_3), 24.1 (CH_3). **Anal. Calcd.** for $C_{27}H_{37}AuCl_2N_2$ (657.47): C, 49.32; N, 4.26; H, 5.67. Found: C, 49.27; N, 4.30; H, 5.69.

*Preparation of [IPrH][AuClBr] (**6**):* A vial was charged with IPr•HBr (50 mg, 0.106 mmol), and [Au(SMe_2)Cl] (31.4 mg, 0.106 mmol). The resulting mixture was dissolved in acetone (0.5 mL) and stirred for 10 min at room temperature. After this time the mixture was filtered through Celite®. The solvent was concentrated and pentane (3 mL) was added, affording a white solid which was washed with further portions of pentane (3 x 1 mL) and dried under vacuum to afford **6** as a white solid in 98% yield (73 mg, 0.104 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 8.98 (t, J = 1.5, 1H, CH_{NCN}), 7.80 (d, J = 1.5, 2H, CH_{imid}), 7.65 (t, J =

7.8, 2H, CH_{Ar}), 7.42 (d, J = 7.8, 4H, CH_{Ar}), 2.41 (sept, J = 6.9, 4H, CH_{iPr}), 1.30 (d, J = 6.9, 12H, CH_3), 1.24 (d, J = 6.8, 12H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 145.5 (C_{Ar}), 137.6 (CH_{NCN}), 133.1 (C_{Ar}), 129.9 (C_{Ar}), 126.7 (CH_{imid}), 125.6 (CH_{Ar}), 29.7 (CH_{iPr}), 25.0 (CH_3), 24.2 (CH_3). **Anal. Calcd**. for $C_{27}H_{37}AuBrClN_2$ (701.92): C, 46.20; N, 3.99; H, 5.31. Found: C, 46.34; N, 4.14; H, 5.45.

*Preparation of [IPrH][AuClI] (**7**):* A vial was charged, under air, with IPr•HI (50 mg, 0.097 mmol), and [Au(SMe_2)Cl] (28.6 mg, 0.097 mmol). The resulting mixture was dissolved in acetone (0.5 mL) and stirred for 10 min at room temperature. After this time the mixture was filtered through Celite®. The solvent was concentrated and pentane (3 mL) was added, affording a white solid which was washed with further portions of pentane (3 x 1 mL) and dried under vacuum to afford **7** as a white solid in 98% yield (71 mg, 0.095 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 8.89 (t, J = 1.5, 1H, CH_{NCN}), 7.81 (d, J = 1.6, 2H, CH_{imid}), 7.66 (t, J = 7.8, 2H, CH_{Ar}), 7.43 (d, J = 7.8, 4H, CH_{Ar}), 2.41 (sept, J = 6.8, 4H, CH_{iPr}), 1.31 (d, J = 6.9, 12H, CH_3), 1.24 (d, J = 6.8, 12H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, CD_2Cl_2): δ 145.5 (C_{Ar}), 137.5 (CH_{NCN}), 133.2 (C_{Ar}), 129.9 (C_{Ar}), 126.7 (CH_{imid}), 125.6 (CH_{Ar}), 29.7 (CH_{iPr}), 25.0 (CH_3), 24.2 (CH_3). **Anal. Calcd.** for $C_{27}H_{37}AuICIN_2$ (748.92): C, 43.30; N, 3.74; H, 4.98. Found: C, 43.37; N, 3.86; H, 5.01.

*Preparation of [Au(IPr)Br] (**8**):* Following the small scale general procedure, a mixture of IPr•HBr (100 mg, 0.213 mmol), [Au(SMe_2)Cl] (62.7 mg, 0.213 mmol) and K_2CO_3 (29.4 mg, 0.213 mmol) in acetone (1.0 mL) was stirred for 2 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 85% yield (121 mg, 0.181 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.57 (t, J = 7.8, 2H, CH_{Ar}), 7.35 (d, J = 7.8, 4H, CH_{Ar}), 7.24 (s, 2H, CH_{imid}), 2.57 (sept, J = 6.9, 4H, CH_{iPr}), 1.34 (d, J = 6.9, 12H, CH_3), 1.23 (d, J = 6.9, 12H, CH_3). **^{13}C{^{1}H} NMR** (75.4 MHz, CD_2Cl_2): δ 179.0 (C_{carb}), 146.3 (C_{Ar}), 134.6 (C_{Ar}), 131.2 (CH_{Ar}), 124.8 (CH_{Ar}), 123.8 (CH_{imid}), 29.3 (CH_{iPr}), 24.7 (CH_3), 24.3 (CH_3). **Anal. Calcd.** for $C_{27}H_{36}AuBrN_2$ (665.46): C, 48.73; N, 4.21; H, 5.45. Found: C, 48.68; N, 4.19; H, 5.57.

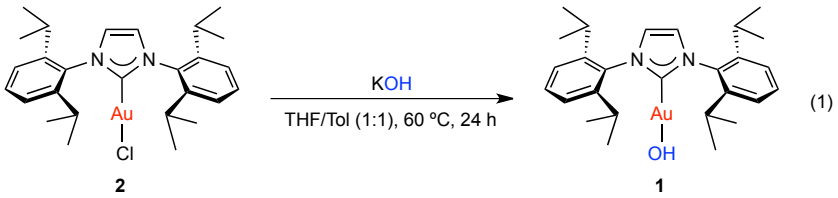
*Preparation of [Au(IPr)I] (**9**):* Following the small scale general procedure, a mixture of IPr•HI (100 mg, 0.194 mmol), [Au(SMe_2)Cl] (57.1 mg, 0.194 mmol) and K_2CO_3 (26.8 mg, 0.194 mmol) in acetone (1.0 mL) was stirred for 2 h at 60 ºC. After the workup, the desired complex was obtained as a white solid in 86% yield (119 mg, 0.167 mmol). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.57 (t, J = 7.8, 2H, CH_{Ar}), 7.35 (d, J = 7.8, 4H, CH_{Ar}), 7.24 (s, 2H, CH_{imid}), 2.58 (sept, J = 6.9, 4H, CH_{iPr}), 1.34 (d, J = 6.9, 12H, CH_3), 1.23 (d, J = 6.9, 12H, CH_3). **^{13}C{^{1}H} NMR** (75.4 MHz, CD_2Cl_2): δ 185.5 (C_{carb}), 146.3 (C_{Ar}), 134.4 (C_{Ar}), 131.2 (CH_{Ar}),

124.7 (CH$_{Ar}$), 123.7 (CH$_{imid}$), 29.3 (CH$_{i\text{Pr}}$), 24.7 (CH$_3$), 24.3 (CH$_3$). **Anal. Calcd.** for $C_{27}H_{36}AuIN_2$ (712.46): C, 45.52; N, 3.93; H, 5.09. Found: C, 45.53; N, 3.87; H, 5.19.

4. Synthetic Routes Towards [Au(NHC)(OH)] Complexes

4.1 Introduction

Pursuing the synthesis of new gold catalysts and following computational studies that predicted the formation of a stable Au^{I}-OH species, we recently reported the synthesis of [Au(IPr)(OH)] (**1**), the first mononuclear Au^{I}-hydroxide complex.[23a] This new gold species was synthesised from [Au(IPr)Cl] (**2**) and KOH in a 1:1 mixture of THF/toluene heated at 60 ºC for 24 h (eq. 1).[23a]



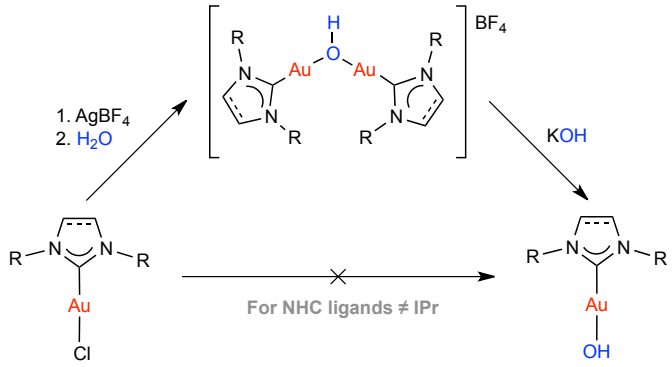
As seen in Chapter 1, hydroxide **1** has proven to be a versatile synthon, granting access to a wide range of novel organogold species under mild conditions.[43,48-50,118] For example, **1** has been successfully used for the activation of acetylenic C-H bonds, generating gold-acetylide complexes,[43] or to synthesise aryl-gold species *via* decarboxylation reactions[48] or reaction with boronic acids[49] and siloxanes.[50] Intrigued by the broad reactivity of **1**,[23a,118c] we forged ahead in this area and investigated the synthesis of new [Au(NHC)(OH)] complexes. Following the existing procedure, thus far only hydroxide **1**, bearing IPr as ancillary ligand, had been easily isolated in pure form. As has often been the case in our studies on NHC ligands, IPr emerged as a privileged member of this family. Moreover, this procedure was found to be poorly scalable. Therefore, in order to exploit the full range of gold-hydroxide chemistry; the development of more robust synthetic pathways able to accommodate a wider range of Au-NHC species was investigated.

4.2 Results and Discussion

4.2.1 *Synthesis of [Au(NHC)(OH)] from [{Au(NHC)}$_2$(μ-OH)][BF$_4$]*

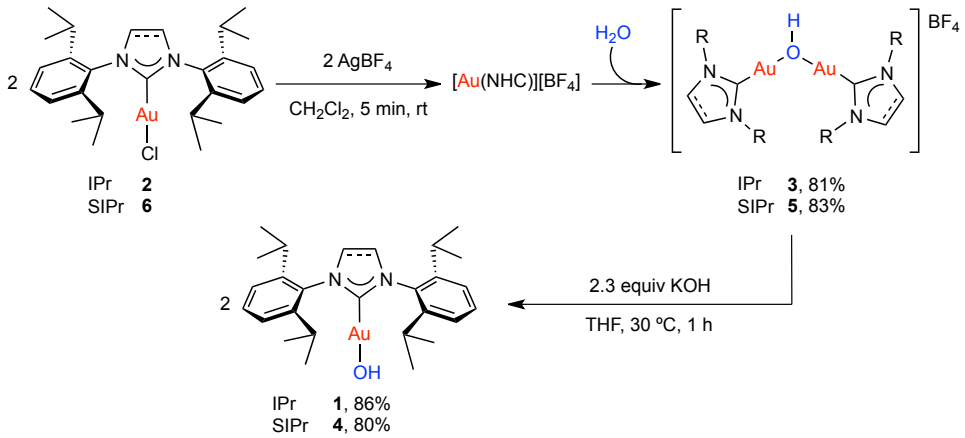
The digold hydroxide complex [{Au(IPr)}$_2$(μ-OH)][BF_4] (**3**), discovered during the course of studies dealing with acid activation of hydroxide **1**,[29] can be formally viewed as being comprised of a cationic $[Au(NHC)]^+$ species coordinated to the oxygen of a Au-hydroxide (see Chapter 1 for more details).[31a] Hence, we envisioned a two-step procedure starting from the chloride precursor [Au(NHC)Cl], generating the digold species [{Au(NHC)}$_2$(μ-OH)][BF_4] and then followed by formation of the [Au(NHC)OH] by addition of KOH

(Scheme 1). In order to test our hypothesis we decided to begin our studies using IPr as the NHC ligand.



Scheme 1. Proposed synthetic route leading to [Au(NHC)(OH)]

First, the digold species **3** was synthesised by addition of $AgBF_4$ to a solution of complex **2** in dichloromethane. After filtration of the AgCl precipitate, addition of water to the intermediate [Au(IPr)][BF_4] afforded the digold complex **3** in 81% yield (Scheme 2). In order to validate our hypothesis that **3** could lead to **1**, 2.3 equiv of KOH were added to a solution of digold complex **3** in THF. THF was chosen as solvent in order to avoid the formation of [Au(NHC)Cl] species by traces of HCl in chlorinated solvents. After stirring for 1 h at 30 ºC, ^{1}H NMR analysis of the reaction mixture confirmed full conversion to gold hydroxide **1** which was isolated in 86% yield. Encouraged by these results and the high stability shown by the digold species, we investigated the generality of the new procedure using a similar NHC ligand. SIPr, the saturated version of IPr, was the ligand of choice and the synthesis of [Au(SIPr)(OH)] (**4**) was next targeted. The digold species [{Au(SIPr)}$_2$(μ-OH)][BF_4] (**5**) was first synthesised. Chloride abstraction from [Au(SIPr)Cl] (**6**) by $AgBF_4$ and subsequent reaction with water, afforded digold species **5** in 83% isolated yield (Scheme 2).



Scheme 2. Synthesis of Au-hydroxides *via* a two-step procedure

The synthesis of hydroxide **4** was next attempted starting from **5**. After a reaction time of 1 h, **4** was isolated in 80% yield (Scheme 2). This reaction represented the first successful synthesis of a Au-hydroxide bearing a NHC ligand other than IPr.

Single crystals suitable for X-ray diffraction studies were obtained by slow diffusion of pentane into a saturated THF solution of **4**. As expected, hydroxide **4** adopts a linear geometry, with a C1-Au-O1 angle of 180.00(1)º, a Au-C1 bond length of 1.976(8) Å and a Au-O1 bond length of 2.019(7) Å. Unfortunately, the H atom corresponding to the OH is disordered, thus no O-H length could be confidently calculated. The Au-C1 bond distance is longer for SIPr complexes than for IPr complexes (1.935(6) Å for hydroxide **1**). This trend can also be observed in the Au-C1 distances of the chloro complexes **2** and **6** (1.942(3) Å for IPr and 1.979(3) Å for SIPr). One way to account for these variations would be the different steric bulk exhibited by each ligand. Computational studies using Samb*V*ca[90] reveal that the $\%V_{Bur}$ is greater for **4** (46.6) than for **1** (43.2).[86] Moreover, the Au-O1 distance is significantly shorter for **4** compared to that found in **1** (2.078(6) Å).

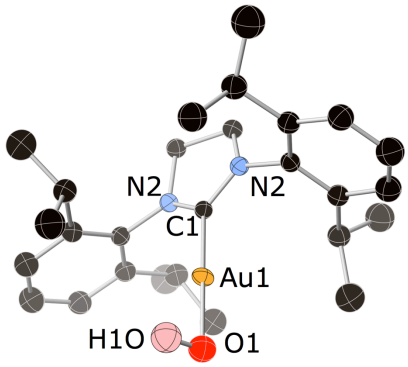
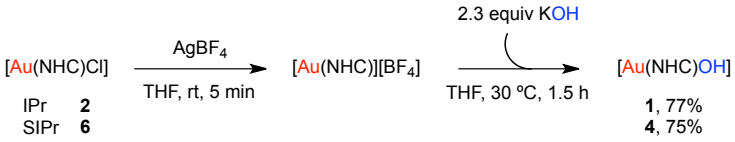


Figure 1. Thermal ellipsoid representation of [Au(SIPr)(OH)] (**4**). Most H atoms are omitted for clarity. Selected bond distances (Å) and angles (º) for 4: Au1–O1 2.019(7), Au1–C1 1.976(8), C1–Au1–O1 180.00(1).

Since this new synthetic route requires the synthesis and isolation of digold hydroxide complexes, the development of a more straightforward procedure was next investigated.

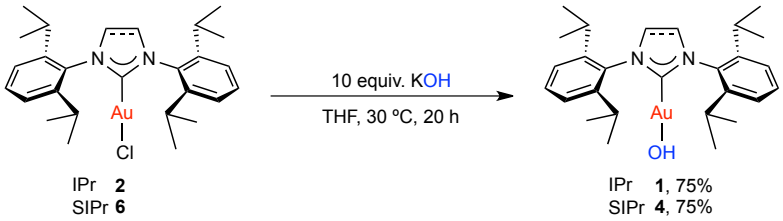
4.2.2 *Synthesis of [Au(NHC)OH] from [Au(NHC)Cl] complexes*

As the reaction proceeded faster and under milder conditions using a cationic species, such as **5**, a one-pot approach was devised around this new strategy. Starting from a chloro complex [Au(NHC)Cl], using $AgBF_4$ as chloride abstractor, the cationic gold species [Au(NHC)][BF_4] was generated. After filtration of the AgCl precipitate, 2.3 equiv. of KOH were next added. We were very pleased to observe that after stirring for 1.5 h at 30 ºC, the reaction was complete and both hydroxides, **1** and **4**, were successfully isolated in 77% and 75% yields, respectively (Scheme 3).



Scheme 3. One-pot synthesis of [Au(NHC)(OH)] from [Au(NHC)Cl] precursors

In order to achieve even more ideal reaction conditions, one further improvement had to be considered: to avoid the use of expensive silver salts. To this end, several chloride abstractors were screened. During the course of this study, a control reaction showed that if a larger excess of KOH was used, silver salts were unnecessary and the reaction reached completion within 20 h. As we could perform the reaction without silver salts, using longer but still acceptable reaction times, the reaction conditions were optimised in THF, stirring for 20 h at 30 ºC, affording both hydroxides, **1** and **4,** in 75% isolated yields (Scheme 4).



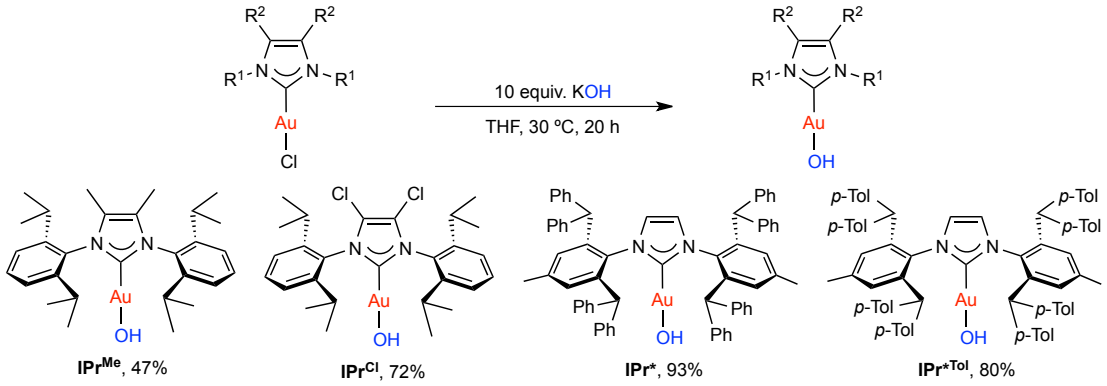
Scheme 4. Optimised reaction conditions for the synthesis of [Au(NHC)OH]

The faster reaction times observed when the reaction was carried out through the intermediacy of the cationic gold species, suggest that the rate-determining step in the reaction is the chloride abstraction from the [Au(NHC)Cl] complex. When efficient chloride abstractors were used, e.g. silver salts, the hydroxide exchange was faster and complexes **1** and **4** were obtained within 2 h; whilst in the absence of an efficient chloride abstractor, the hydroxide exchange was slower and the reaction required at least 20 h. Moreover, we suspected that the problem encountered with the synthesis of Au-hydroxides bearing NHC ligands other than IPr is the thermal stability of the intermediate species generated during the reaction. In the original procedure for the synthesis of hydroxide **1**, it was necessary to heat the reaction to 60 ºC,[23a] whilst in the present procedure, the temperature was reduced to 30 ºC but required the use of a larger amount of KOH.

In order to validate the scalability of the new excess KOH procedure, complexes **1** and **4** were synthesised on a 1 g scale. Gratifyingly, both reactions reached completion within 24 h, affording gold hydroxides **1** and **4**, in 75% and 70% isolated yields, respectively.

Encouraged by the excellent results obtained with SIPr we proceeded to evaluate the viability of this new methodology by extending it to other Au-hydroxide complexes bearing different NHC ligands. Due to their structural similarities to IPr, the following NHCs ligands

were examined: IPr^{Me}, IPr^{Cl}, IPr* and IPr^{*Tol}. Gratifyingly, all the reactions proceeded smoothly and the corresponding [Au(NHC)OH] were isolated in moderate to excellent yields (47-93%) (Scheme 5).



Scheme 5. Synthesis of several [Au(NHC)OH] species

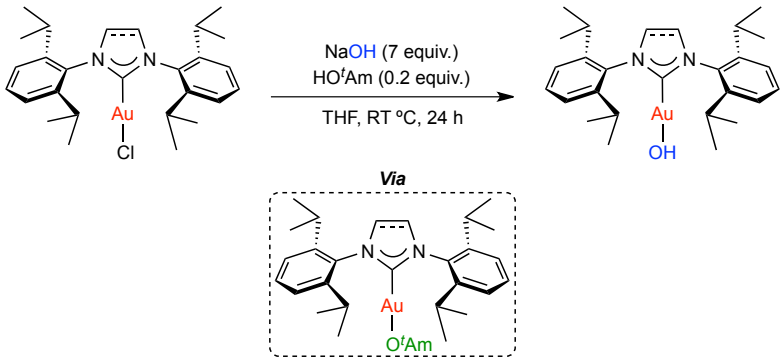
Unfortunately, when we attempted to expand this methodology beyond IPr based ligands we were not able to isolate pure Au-hydroxide complexes. We believe that the steric hindrance offered by the NHC ligand plays a key role in the stabilisation of Au-hydroxide species. While [Au(NHC)OH] complexes were easily synthesised using bulky NHC ligands, such as the IPr based ones (%V_{bur} ~ 44-51), the use of smaller NHCs, such as ICy or IMes (%V_{bur} ~ 27-37), resulted in complex mixtures of [Au(NHC)Cl], [Au(NHC)OH] and decomposition products, thus suggesting that bulkier NHC ligands are better suited for the synthesis of Au-OH species.

4.3 Conclusions

A new strategy for the synthesis of Au^{I}-hydroxide complexes was reported and, through optimisation, insights into the reaction mechanism leading to the formation of the gold hydroxides were provided. A two-step procedure starting from [Au(NHC)Cl], generating [{Au(NHC)}$_2$(μ-OH)][BF_4] and subsequent addition of KOH, afforded [Au(NHC)(OH)] in good yields (80-86%) within short reaction times (1 h). This procedure enabled the isolation of the novel [Au(SIPr)(OH)]. A one-pot reaction, without the isolation of a digold species, was also developed. Reaction *via* the cationic species [Au(NHC)][BF_4] also allowed the formation of gold hydroxides in good yields (75-77%) and short reaction times (1.5 h). In order to avoid using expensive silver salts, [Au(NHC)(OH)] (NHC = IPr and SIPr) were successfully isolated in good yields using a simpler protocol, whereas a larger amount of KOH was employed. However, longer reaction times were required due to the inefficient chloride abstraction performed by KOH under these conditions. In the end, for synthetic purposes Ockham's razor prevails,[119] *simpler is better* and only a larger excess of KOH

appears to solve issues of scalability and reproducibility previously encountered. This procedure was then successfully extended to other Au-NHC complexes such as IPr^{Me}, IPr^{Cl}, IPr* and IPr^{*Tol}. Unfortunately, attempts to expand this methodology beyond IPr based ligands were unsuccessful. We suspected that this was related to the need of bulky NHC ligands in order to stabilise the OH moiety. This hypothesis was later confirmed by another member of our research group.[23b] He was able to synthesise several Au-OH bearing smaller NHC ligands; however, inert conditions were required.

Our group has recently reported a new synthetic route for the preparation of [Au(NHC)OH] complexes (NHC = IPr derivatives) which allows the synthesis of such species on multi-gram scale, e.g. up to 20 g of [Au(IPr)OH] have been prepared, *via* a gold-alkoxide intermediate (Scheme 6).[120]



Scheme 6. Optimised multi-gram scale procedure for the synthesis of gold hydroxides

4.4 Experimental Section

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. Deuterated solvents (CD_2Cl_2, $CDCl_3$) were filtered through basic alumina in order to remove traces of HCl. NMR spectra were recorded on 500, 400 and 300 MHz spectrometers at room temperature in C_6D_6, CD_2Cl_2 or $CDCl_3$. Chemical shifts are given in parts per million (ppm) with respect to TMS. Elemental analyses were carried out by the analytical services of London Metropolitan University. CCDC 856432 (**4**) contains the supplementary crystallographic data for this chapter. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

General procedure for the synthesis of [{Au(NHC)}$_2$(μ-OH)][BF$_4$] complexes: $AgBF_4$ (40 mg, 0.20 mmol) was added to a stirred solution of [Au(NHC)Cl] (100 mg, 0.16 mmol) in dichloromethane (5 mL). The reaction mixture was stirred in the dark at room temperature for

5 min and then filtered over Celite® into a separating funnel containing distilled water (10 mL). The mixture was shaken for 1 min and the organic phase was collected, dried over anhydrous $MgSO_4$ and concentrated under vacuum. The resulting solid was dissolved in the minimum amount of CH_2Cl_2 (2 mL) and the product was precipitated by addition of 8 mL of pentane. The precipitate was collected by filtration, affording the corresponding [{Au(NHC)}$_2$(μ-OH)][BF_4] species as a white powder.

Synthesis of [{Au(IPr)}$_2$(μ-OH)][BF_4] (**3**): Following the general procedure, 81% of a white powder was obtained. NMR data matched the literature.[29,31a] **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.50 (t, *J* =7.8 Hz, 4H, C*H*$_{Ar}$), 7.26 (s, 4H, C*H*$_{imid}$), 7.24 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 2.39 (sept, *J* = 6.9 Hz, 8H, C*H*$_{i\text{Pr}}$), 1.19 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 1.11 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 0.28 (s, 1H, OH) ppm. **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$): δ = 162.6 (*C*$_{carb}$), 145.4 (*C*$_{Ar}$), 133.6 (*C*$_{Ar}$), 130.7 (*C*H$_{Ar}$), 124.2 (*C*H$_{Ar}$), 124.1 (*C*H $_{imid}$), 28.6 (*C*H$_{i\text{Pr}}$), 24.4 (*C*H$_3$), 23.8 (*C*H$_3$) ppm. **^{19}F{^{1}H} NMR** (185 MHz, $CDCl_3$): δ = -154.90, -154.85 ppm.

Synthesis of [{Au(SIPr)}$_2$(μ-OH)][BF_4] (**5**): Following the general procedure, 83% of a white powder was obtained. **^{1}H NMR** (400 MHz; CD_2Cl_2): δ = 7.42 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.19 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 4.01 (s, 8H, C*H*$_2$ $_{imid}$), 2.88 (sept, *J* = 6.9 Hz, 8H, C*H*$_{i\text{Pr}}$), 1.28 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 1.16 (d, *J* = 6.8 Hz, 24H, C*H*$_3$), 0.37 (s, 1H, OH) ppm. **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ = 186.1 (*C*$_{carb}$), 146.9 (*C*$_{Ar}$), 134.1 (*C*$_{Ar}$), 130.4 (*C*H$_{Ar}$), 124.9 (*C*H$_{Ar}$), 53.93 (*C*H$_2$ $_{imid}$), 53.80 (*C*H$_2$ $_{imid}$), 29.1 (*C*H$_{i\text{Pr}}$), 25.2 (*C*H$_3$), 24.1 (*C*H$_3$) ppm. **^{19}F{^{1}H} NMR** (376 MHz; CD_2Cl_2): δ = -154.09, -154.14 ppm. **Anal. Calcd.** for $C_{54}H_{77}Au_2BF_4N_4O$ (1278.95): C, 50.71; H, 6.07; N, 4.38. Found: C, 50.58; H, 6.00; N, 4.49.

Syntheses of [Au(SIPr)(OH)] (**4**)

From [{Au(SIPr)}$_2$(μ-OH)][BF_4] (**5**)*:* KOH (10 mg, 0.18 mmol) was added to a solution of [{Au(SIPr)}$_2$(μ-OH)][BF_4] (**5**) (100 mg, 78 μmol) in THF (3 mL). The reaction mixture was stirred for 1 h at 30 ºC, then filtered over Celite® and concentrated under vacuum. The resulting solid was dissolved in 2 mL of THF and the product was precipitated by addition of 8 mL of pentane. The precipitate was collected by filtration, affording **4** in 86% yield as a white powder.

From [Au(SIPr)Cl] using $AgBF_4$: $AgBF_4$ (40 mg, 0.20 mmol) was added to a solution of [Au(SIPr)Cl] (**6**) (100 mg, 0.16 mmol) in THF (3 mL). The reaction mixture was stirred avoiding the presence of light at room temperature for 5 min and then filtered over Celite®. KOH (20.6 mg, 0.368 mmol) was then added. The reaction was stirred for 1.5 h at 30 ºC,

filtered over Celite® and concentrated under vacuum. The resulting solid was dissolved in 2 mL of THF and the product was precipitated by addition of 10 mL of pentane. The precipitate was collected by filtration, affording **4** in 75% yield as a white powder.

From [Au(SIPr)Cl] using KOH: KOH (90 mg, 1.6 mmol) was added to a solution of [Au(SIPr)Cl] (**6**) (100 mg, 0.16 mmol) in THF (3 mL). The reaction mixture was stirred for 20 h at 30 ºC, then filtered over Celite® and concentrated under vacuum. The resulting solid was dissolved in 2 mL of THF and the product was precipitated by addition of 10 mL of pentane. The precipitate was collected by filtration, affording **4** as a white powder in 75% yield. **^{1}H NMR** (400 MHz; CD_2Cl_2): δ = 7.45 (t, *J* = 7.8 Hz, 2H, C*H*$_{Ar}$), 7.28 (d, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 3.99 (s, 4H, C*H*$_{2\ imid}$), 3.06 (sept, *J* = 6.9 Hz, 4H, C*H*$_{i Pr}$), 1.41 (d, *J* = 6.8 Hz, 12H, C*H*$_3$), 1.33 (d, *J* = 6.9 Hz, 12H, C*H*$_3$), -0.71 (br, 1H, OH) ppm. **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ = 193.5 (*C*$_{carb}$), 147.2 (*C*$_{Ar}$), 135.0 (*C*$_{Ar}$), 130.0 (*C*H$_{Ar}$), 124.8 (*C*H$_{Ar}$), 53.7 (*C*H$_{2\ imid}$), 29.2 (*C*H$_{i Pr}$), 25.1 (*C*H$_3$), 24.2 (*C*H$_3$) ppm. **Anal. Calcd.** for $C_{27}H_{39}AuN_2O$ (604.58): C, 53.64; H, 6.50; N, 4.63. Found: C, 53.50; H, 6.36; N, 4.48.

General procedure for the synthesis of [Au(NHC)(OH)]: Potassium hydroxide (10 equiv.) was added to a solution of [Au(NHC)Cl] (1 equiv.) in THF. The mixture was stirred at 30 °C for 20 h, and then filtered through Celite®. Then, the solution was concentrated, and the product precipitated by addition of pentane and collected by filtration.

[Au(IPr^{Me})(OH)]: Following the general procedure using [Au(IPr^{Me})Cl] (250 mg, 0.385 mmol), KOH (216 mg, 3.85 mmol) and THF (3 mL). [Au(IPr^{Me})(OH)] was obtained as a white, microcrystalline solid (115 mg, 47%). **^{1}H NMR** (300 MHz, C_6D_6): δ 7.23 (t, *J* = 7.5 Hz, 2H, C*H*$_{Ar}$), 7.07 (d, *J* = 7.5 Hz, 4H, C*H*$_{Ar}$), 2.54 (sept, *J* = 7.0 Hz, 4H, C*H*$_{i Pr}$), 1.49 (d, *J* = 7.0 Hz, 12H, C*H*$_3$), 1.41 (s, 6H, C*H*$_{3\ imid}$), 1.06 (d, *J* = 7.0 Hz, 12H, C*H*$_3$), - 0.32 (br, 1H, OH) ppm. **^{13}C{^{1}H} NMR** (100 MHz, C_6D_6): δ 170.4 (*C*$_{carb}$), 146.2 (*C*$_{Ar}$), 133.3 (*C*$_{Ar}$), 130.7 (C*H*$_{Ar}$), 125.5 (*C*CH$_{3\ imid}$), 124.5 (C*H*$_{Ar}$), 29.0 (*C*H$_{i Pr}$), 25.1 (*C*H$_3$), 23.5 (*C*H$_3$), 9.3 (C*C*H$_{3\ imid}$) ppm. **Anal. Calcd** for $C_{29}H_{41}AuN_2O$ (631.62): C, 55.23; H, 6.55; N, 4.44. Found: C, 55.31; H, 6.65; N, 4.43.

[Au(IPr^{Cl})(OH)]: Following the general procedure using [Au(IPr^{Cl})Cl] (1.00 g, 1.45 mmol), KOH (814.3 mg, 14.5 mmol) and THF (5 mL). [Au(IPr^{Cl})(OH)] was obtained as a white, microcrystalline solid (700 mg, 72%). **^{1}H NMR** (400 MHz, C_6D_6): δ 7.20 (t, *J* = 8.0 Hz, 2H, C*H*$_{Ar}$), 7.03 (d, *J* = 8.0 Hz, 4H, C*H*$_{Ar}$), 2.58 (sept, *J* = 6.6 Hz, 4H, C*H*$_{i Pr}$), 1.42 (d, *J* = 6.8 Hz, 12H, C*H*$_3$), 1.09 (d, *J* = 6.8 Hz, 12H, C*H*$_3$), −0.23 (br, 1H, OH) ppm. **^{13}C{^{1}H} NMR** (100 MHz, C_6D_6): δ 175.0 (*C*$_{carb}$), 146.4 (*C*$_{Ar}$), 131.9 (*C*$_{Ar}$), 131.6 (C*H*$_{Ar}$), 124.7 (C*H*$_{Ar}$), 118.3

(*C*Cl $_{imid}$), 29.5 (*C*H$_{iPr}$), 24.6 (*C*H$_3$), 23.4 (*C*H$_3$) ppm. **Anal. Calcd** for $C_{27}H_{35}AuN_2O$ (672.46): C, 48.30; H, 5.25; N, 4.17. Found: C, 48.47; H, 5.37; N, 4.26.

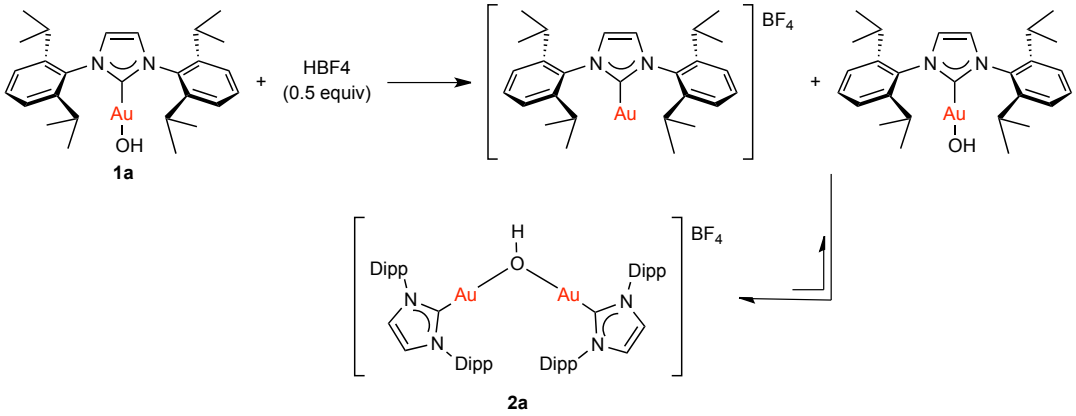
[Au(IPr)(OH)]*: Following the general procedure using [Au(IPr*)Cl] (500 mg, 0.436 mmol), KOH (244.8 mg, 4.36 mmol) and THF (3 mL). [Au(IPr*)(OH)] was obtained as a white, microcrystalline solid (459 mg, 93%). **^{1}H NMR** (500 MHz, CD_2Cl_2): δ 7.24-7.14 (m, 32H C*H*$_{Ar}$), 6.93 (s, 4H), 6.87 (dd, J = 6.6, 2.9 Hz, 8H), 5.75 (s, 2H), 5.32 (s, 4H), 2.26 (s, 6H), - 0.35 (br, 1H, OH). **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ 172.3 (*C*$_{carb}$), 143.2 (*C*$_{Ar}$), 143.1 (*C*$_{Ar}$), 141.3 (*C*$_{Ar}$), 140.5 (*C*$_{Ar}$), 134.4 (C*H*$_{Ar}$), 130.5 (C*H*$_{Ar}$), 130.3 (C*H*$_{Ar}$), 130.1 (C*H*$_{Ar}$), 129.6 (C*H*$_{Ar}$), 128.8 (C*H*$_{Ar}$), 127.0 (C*H*$_{Ar}$), 127.0 (C*H*$_{Ar}$), 123.3 (*C*H $_{imid}$), 51.6 (*C*HPh$_2$), 21.9 (*C*H$_3$) ppm. **Anal**. **Calcd** for $C_{69}H_{57}AuN_2O$ (1128.18): C, 73.52; H, 5.10; N, 2.49. Found: C, 73.39; H, 4.97; N, 2.34.

[Au(IPr^{Tol})(OH)]*: Following the general procedure using [Au(IPr*^{Tol})Cl] (200 mg, 0.160 mmol), KOH (90 mg, 1.60 mmol) and THF (3 mL). [Au(IPr*^{Tol})(OH)] was obtained as a white, microcrystalline solid (158 mg, 80%). **^{1}H NMR** (500 MHz, CD_2Cl_2): δ 7.07-7.01 (m, 16H, C*H*$_{Tol}$), 6.97 (d, J = 7.9 Hz, 8H, C*H*$_{Tol}$), 6.92 (s, 4H, C*H*$_{Ar}$), 6.74 (d, J = 7.9 Hz, 8H, C*H*$_{Tol}$), 5.79 (s, 2H, C*H*$_{imid}$), 5.22 (s, 4H, C*H*Tol$_2$), 2.30 (s, 12H, C*H*$_{3\ Tol}$), 2.28 (s, 12H, C*H*$_{3\ Tol}$), 2.26 (s, 6H, C*H*$_{3\ Ar}$), - 0.44 (br, 1H, OH). **^{13}C{^{1}H} NMR** (100 MHz; CD_2Cl_2): δ 171.8 (*C*$_{carb}$), 141.6 (*C*$_{Ar}$), 140.4 (*C*$_{Ar}$), 140.4 (*C*$_{Tol}$), 140.2 (*C*$_{Tol}$), 136.5 (*C*$_{Ar}$), 136.5 (*C*$_{Tol}$), 134.3 (*C*$_{Ar}$), 130.2 (C*H*$_{Ar}$), 129.9 (C*H*$_{Ar}$), 129.5 (C*H*$_{Tol}$), 129.3 (C*H*$_{Tol}$), 123.3 (*C*H $_{imid}$), 50.8 (*C*HTol$_2$), 21.9 (*C*H$_{3\ Ar}$), 21.1 (*C*H$_{3\ Tol}$), 21.0 (*C*H$_{3\ Tol}$) ppm. **Anal. Calcd.** for $C_{77}H_{73}AuN_2O$ (1240.39): C, 74.62; H, 5.94; N, 2.26. Found: C, 74.53; H, 6.02; N, 2.33.

5. [{Au(NHC)}$_2$(μ-OH)][BF$_4$] as *Silver-Free* Catalysts

5.1 Introduction

Generally, organogold(I) species are linear, two-coordinate complexes of the formula [Au(L)Cl], where L = phosphine or *N*-heterocyclic carbene (NHC) ligands.[2a,2c-e,5a,121] The use of a halide abstractor, usually a silver salt, is necessary in order to generate the active catalyst from Au(I)-halide complexes.[2a,2c-e,5a,121] This procedure has several drawbacks, such as the high price of the silver salt activator, the light sensitivity of these silver salts, and the fact that silver can itself be a catalyst, oftentimes exhibiting a different reactivity profile that can modify the otherwise *gold-only* catalysed reaction.[21] For these reasons the development of new silver-free protocols has become an important issue in gold catalysis. As seen in previous chapters, our group has recently contributed to this field with the synthesis of a gold-hydroxide species [Au(IPr)(OH)] (**1a**) that can be easily activated by an acid, e.g. HBF$_4$ or HSbF$_6$, to generate the active species [Au(IPr)]$^+$.[29-30,51b] In the course of these studies a diaurated species of the formula [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (**2a**) was discovered (Scheme 1).[29]



Scheme 1. Reaction sequence leading to the formation of the diaurated species **2a**.

To the best of our knowledge, only a handful of digold-hydroxide complexes of the formula [{Au(L)}$_2$(μ-OH)][X] have been reported to date (Figure 1). We have reported the synthesis and characterisation of **2a** and [{Au(SIPr)}$_2$(μ-OH)][BF$_4$] (**2b**) (see Chapter 4 for more information), while Maier and co-workers have recently disclosed the synthesis of two diaurated complexes bearing Buchwald-type phosphine ligands and [{Au(IMes)}$_2$(μ-OH)][BF$_4$].[122] However, only the catalytic activity of the IPr derivative **2a** has been studied.[29,31a,51b] This diaurated complex has proven to be highly active in a number of water-inclusive gold-catalysed transformations, such as alkyne hydration, nitrile hydration and the

Meyer-Schuster rearrangement, all these being conducted without any additives to induce catalyst activation.[29,31a,51b]

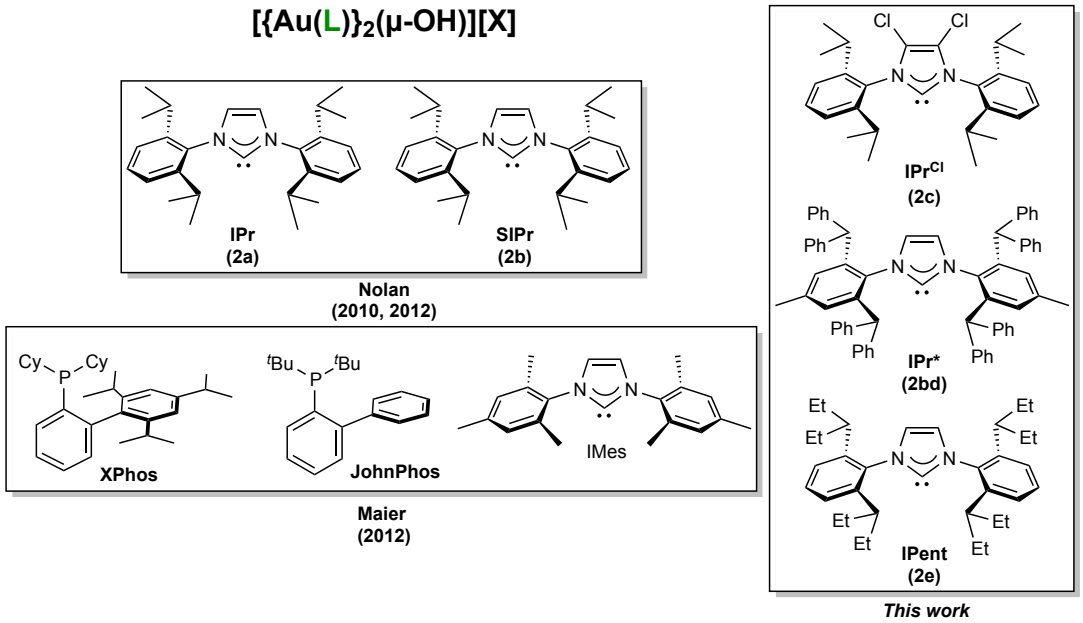


Figure 1. [{Au(L)}$_2$(μ-OH)][X] (L = NHC or PR$_3$) complexes reported to date.

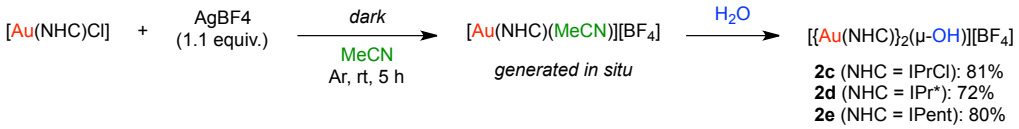
With these early results in hand, we decided to expand the library of diaurated hydroxide complexes and test their catalytic activity in order to illustrate the feasibility of silver-free, acid-free gold-catalysed methodologies. In this Chapter we report the synthesis of three new [{Au(NHC)}$_2$(μ-OH)][BF$_4$] complexes bearing IPr^{Cl} (**2c**), IPr* (**2d**) and IPent (**2e**) ligands, and a study of their respective catalytic activity in several gold-catalysed transformations which permits a comparison to that of the previously reported IPr (**2a**) and SIPr (**2b**) derivatives.

5.2 Results and Discussion

5.2.1 *Synthesis and Characterization*

As described in Chapter 1, there are two main routes for the synthesis of [{Au(NHC)}$_2$(μ-OH)][BF$_4$] complexes: a) reaction of [Au(NHC)(OH)] with 0.5 equiv. of a strong acid, such as HBF$_4$,[29,31a] or b) chloride abstraction from [Au(NHC)Cl] by a silver salt, e.g. AgBF$_4$, in acetonitrile, forming the corresponding [Au(NHC)(MeCN)][BF$_4$] complex in situ, and subsequent addition of water.[123] At the time that this study was performed, the corresponding [Au(NHC)(OH)] complexes had not been described yet, therefore, for synthetic purposes the route used in the present study was the latter methodology. According to this procedure the following complexes were obtained in good yields: [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] (**2c**) 81%, [{Au(IPr*)}$_2$(μ-OH)][BF$_4$] (**2d**) 72% and [{Au(IPent)}$_2$(μ-OH)][BF$_4$] (**2e**) 80% (Scheme 1).

The diaurated nature of complexes **2c-2e** was confirmed by ^{1}H and ^{13}C{^{1}H} NMR spectroscopy as well as by elemental analysis. Compounds **2c** and **2e** present the characteristic OH resonance between 0-1 ppm in the ^{1}H NMR spectrum, while for the IPr* derivative **2d** a significant shift towards higher fields was observed, - 0.74 ppm (NMR spectra recorded in CD_2Cl_2). This chemical shift may be due to the high steric hindrance provided by the IPr* ligand. Unfortunately, attempts to obtain crystals suitable for X-ray diffraction analysis, to further study the structural features of complexes **2c-e**, were unsuccessful.



Scheme 2. Synthesis of Digold Complexes **2c-e.**

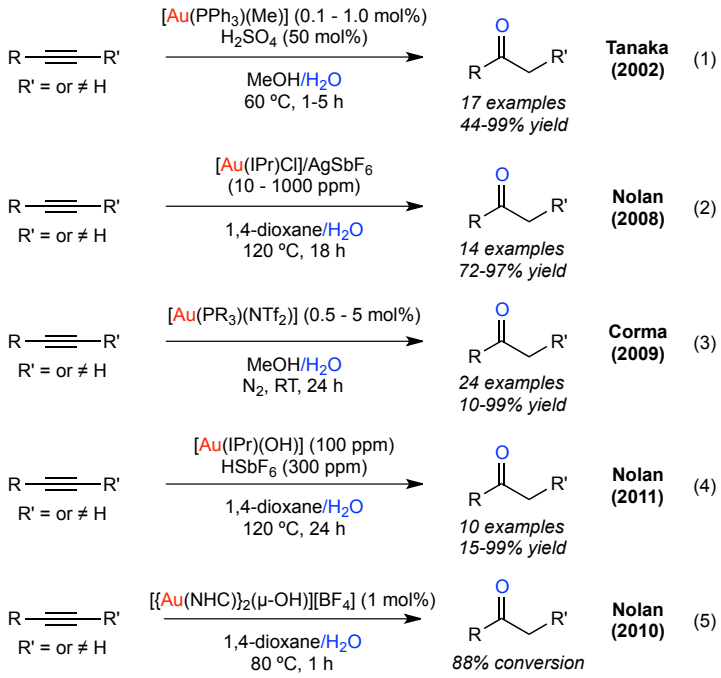
5.2.2 *Catalytic Studies*

As [{Au(NHC)}$_2$(μ-OH)][BF_4] complexes have been postulated as possible catalytic intermediates for gold-catalysed water-inclusive transformations,[29,31a] their activity was tested in alkyne and nitrile hydration, as well as in the Meyer-Schuster rearrangement. In order to confirm their utility as a source of [Au(IPr)]$^+$ when activated by an acid, their catalytic activity was also investigated in the rearrangement of allylic acetates.

5.2.2.1 Alkyne Hydration

The hydration of alkynes to obtain carbonyl derivatives represents one of the most environmentally friendly and atom economical procedures for the formation of C=O bonds.[124] The importance of this reaction is related to the significant impact of the carbonyl motif in organic synthesis.[125,126] Alkyne hydration can be catalysed by either Brønsted acids or by a variety of transition metal complexes.[127] Among the latter, organogold species stand out as some of the most efficient and mild catalysts (Scheme 3).[30a,128] In 2002, Tanaka and co-workers reported the first gold(I)-catalysed alkyne hydration using [Au(PPh_3)(Me)] (0.1-1.0 mol%) and 50% sulfuric acid in methanol as the catalytic system (eq. 1, Scheme 3).[128a] Despite the efficiency of this ground-breaking methodology, the use of such large quantities of a strong acid was bothersome. In 2008, our group reported the hydration of alkynes at very low catalyst loadings (10-1000 ppm) using [Au(IPr)Cl]/$AgSbF_6$ in a mixture of 1,4-dioxane/H_2O as the catalytic system (eq. 2, Scheme 3).[128c] This novel procedure replaced the use of concentrated solutions of strong acids for a stoichiometric amount (relative to the catalyst) of a silver salt to activate the gold complex. In 2009, Corma reported the first acid-free, silver-free gold(I)-catalysed alkyne hydration using Gagosz-type complexes[22] [Au(L)(NTf_2)] (where L = SPhos, PPh_3 or P^{t}Bu$_3$) at room temperature (eq. 3, Scheme 3).[128d]

Despite the milder reaction conditions, this new methodology required the use of higher catalyst loadings (0.5-5 mol%) and longer reaction times.[128d] With the aim of developing new silver-free protocols, our group have recently reported the use of gold hydroxide **1a** activated by an excess of acid (3 equiv. respect to gold) at low catalyst loadings (100-1000 ppm) (eq. 4, Scheme 3).[30a] Digold hydroxide complexes have also been shown to be suitable catalysts for silver-free and acid-free alkyne hydration (eq. 5, Scheme 3).[29]

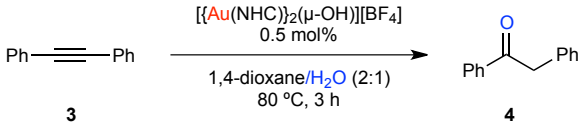


Scheme 3. Selected examples of gold-catalysed alkyne hydration.

In order to test the catalytic activity of the new complexes and compare them with the previously reported catalytic results, we next performed the hydration of alkynes in a mixture of 1,4-dioxane/H_2O (2:1) at 80 ºC for 3 h. Diphenylacetylene (**3**) was chosen as the substrate, because it is one of the most challenging substrates for this transformation. To challenge our catalysts, relatively low catalyst loadings (0.5 mol%) were employed. As shown in Table 1, IPr* complex **2d** performed poorly in this transformation, with only 55% conversion to the desired ketone (**4**) after 3 h (Table 1, entry 4). Complexes **2b** and **2e**, bearing SIPr and IPent ligands, respectively, furnished similar enhanced reactivity (74-83%, Table 1, entries 2 and 5). The IPr derivative **2a** and the newly synthesised IPr^{Cl} complex **2c** were the best catalysts for the hydration of diphenylacetylene, with 92% and 91% conversions respectively (Table 1, entries 1 and 3). In order to determine which of the two complexes, **2a** or **2c**, was the most active, experiments at lower catalyst loadings were performed (Table 1, entries 6-8). To the best of our knowledge, the best reported results for the hydration of diphenylacetylene at low catalyst loadings were obtained using 0.1 mol% of either [Au(IPr)Cl]/$AgSbF_6$ or

[Au(IPr)OH]/HBF$_4$ at 120 ºC for 24 h, with conversions between 70-77%.[30a,128c] Gratifyingly, the desired product, **4**, was obtained in 90% yield under the same reaction conditions using 0.05 mol% of **2c** (Table 1, Entry 8). This result highlights that the digold species [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] **2c** is the best catalyst for the hydration of challenging alkynes at low catalyst loadings reported to date.

Table 1. Gold-catalysed Alkyne Hydration[a]



3 **4**

Entry	Catalyst (mol%)	Conversion (%)[b]
1	**2a** [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (0.5)	92
2	**2b** [{Au(SIPr)}$_2$(μ-OH)][BF$_4$] (0.5)	83
3	**2c** [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] (0.5)	91
4	**2d** [{Au(IPr*)}$_2$(μ-OH)][BF$_4$] (0.5)	55
5	**2e** [{Au(IPent)}$_2$(μ-OH)][BF$_4$] (0.5)	74
6[c]	**2a** [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (0.1)	57
7[c]	**2c** [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] (0.1)	95
8[d]	**2c** [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] (0.05)	95 (90)

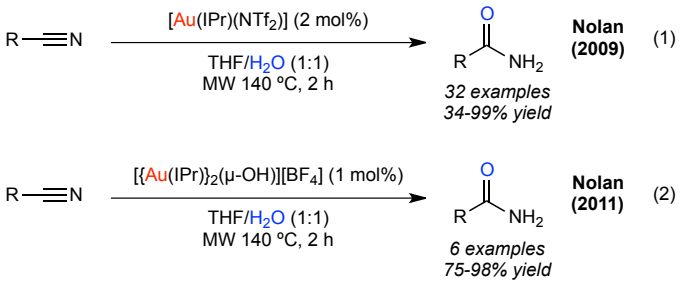
[a] Reaction conditions: [Au] (2.5 μmol), **3** (0.5 mmol) in a mixture of 1,4-dioxane/H$_2$O (2:1, 2 mL), 80 ºC, 3 h. [b] Conversions determined by GC. Average of at least 2 runs. Isolated yield in parentheses. [c] Reaction conditions: [Au] (1.25 μmol), **3** (1.25 mmol) in a mixture of 1,4-dioxane/H$_2$O (2:1, 5 mL), 120 ºC, 24 h. [d] Reaction conditions: [Au] (1.25 μmol), **3** (2.50 mmol) in a mixture of 1,4-dioxane/H$_2$O (2:1, 10 mL), 120 ºC, 24 h.

Our findings are in direct contrast with the recent contribution by Shi and co-workers regarding the "*silver effect*" in gold catalysis. In fact, Shi claims that the gold-catalysed alkyne hydration *cannot* be catalysed only by [Au]$^+$ and that the presence of silver is required for the reaction to proceed.[15] As is the case for Corma's system (eq. 3, Scheme 3)[128d] and our previous contribution on silver-free protocols (eq. 5, Scheme 3),[29] here *no additive* (acid, silver) is required to perform the catalytic reaction. Therefore, the claim that the gold-catalysed alkyne hydration cannot proceed in the absence of silver can be refuted.

5.2.2.2 Nitrile Hydration

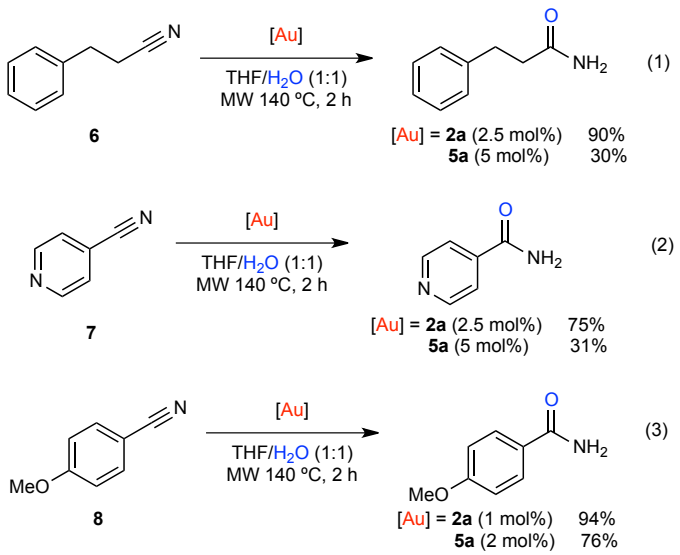
The hydration of nitriles represents the most atom economic synthetic pathway towards the formation of amides.[129] This procedure has been described as catalysed by all the transition metals of Groups 8-11, including gold.[129] However, only two catalytic systems based on this metal have been reported (Scheme 4).[31a,130] Our group described the first gold-catalysed nitrile hydration in 2009.[130] Moderate to excellent yields (34-99%) were obtained using the well-defined Gagosz-type complex [Au(IPr)(NTf$_2$)] (**5a**)[22a] in reactions conducted in

a mixture of THF/H_2O (10:1) at 140 ºC for 2 h under microwave irradiation (eq. 1, Scheme 4).[130] After this initial study, and once the digold species **2a** had been synthesised, it was postulated as a potential key intermediate in this process.[31a] Using 1 mol% of **2a** as catalyst, it was possible to obtain excellent conversions (75-98%) (eq. 2, Scheme 4).[131]



Scheme 4. Previously reported gold-catalysed nitrile hydration

Moreover, the use of **2a** as catalyst afforded substantial improvements for three particularly troublesome substrates (Scheme 5): 3-phenylpropanenitrile (**6**, eq. 1), isonicotinonitrile (**7**, eq. 2), and *p*-methoxybenzonitrile (**8**, eq. 3).[31a] The conversions for **6** and **7** increased by around 60 and 40% respectively when **2a** was used as catalyst instead of the monomeric species **5a**.[31a] In the case of **6**, the conversion increased by 20%. Encouraged by these results, the new catalysts were tested in this transformation.

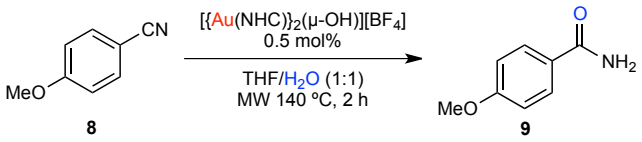


Scheme 5. Comparison between **2a** and **5a** in nitrile hydration of troublesome substrates

Since the reactions involving **6** and **7** required higher catalyst loadings, *p*-methoxybenzonitrile (**8**) was the substrate of choice. The experiments were carried out under the conditions mentioned above, but using lower catalyst loadings (0.5 mol%) (Table 2). As in the case of the alkyne hydration, the complex bearing IPr* **2d** performed poorly in this

reaction affording only 53% conversion to amide **9** after 2 h (Table 2, entry 4). On the other hand, the reactions using **2a-2c** and **2d** gave excellent conversions, between 86-92% (Table 2, entries 1-3 and 5). In order to determine which was the most active complex, experiments at lower catalyst loadings were performed. Gratifyingly, a difference in reactivity could be observed at 0.25 mol%. While the IPr^{Cl} **2c** and IPent **2e** derivatives provided moderate conversions, below 60% (Table 2, entries 7 and 8), the SIPr derivative **2b** was the most active catalyst with 70% conversion (Table 2, entry 6), and is therefore the catalyst of choice for gold-catalysed nitrile hydration reactions.

Table 2. Gold-catalysed Nitrile Hydration[a]



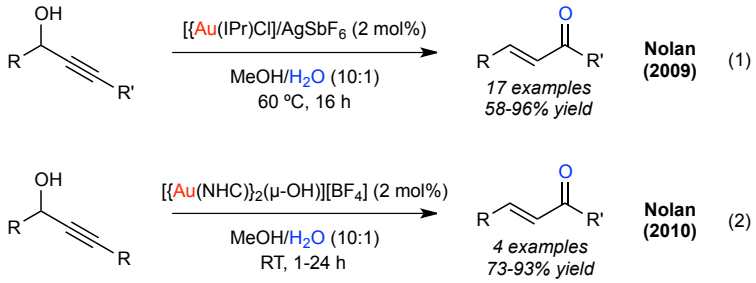
8 **9**

Entry	Catalyst (mol%)	Conversion (%)[b]
1	**2a** [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (0.5)	86
2	**2b** [{Au(SIPr)}$_2$(μ-OH)][BF$_4$] (0.5)	92 (90)
3	**2c** [{Au(IPrCl)}$_2$(μ-OH)][BF$_4$] (0.5)	91
4	**2d** [{Au(IPr*)}$_2$(μ-OH)][BF$_4$] (0.5)	53
5	**2e** [{Au(IPent)}$_2$(μ-OH)][BF$_4$] (0.5)	90
6[c]	**2b** [{Au(SIPr)}$_2$(μ-OH)][BF$_4$] (0.25)	70
7[c]	**2c** [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] (0.25)	59
8[c]	**2e** [{Au(IPent)}$_2$(μ-OH)][BF$_4$] (0.25)	57

[a] Reaction conditions: [Au] (2.5 μmol), **8** (0.5 mmol) in a mixture of THF/H_2O (1:1, 1 mL), 140 ºC, 2 h. [b] Conversions determined by ^{1}H NMR. Average of at least 2 runs. Isolated yield in parentheses. [c] Reaction conditions: [Au] (1.25 μmol), **8** (0.5 mmol) in a mixture of THF/H_2O (1:1, 1 mL), 140 ºC, 2 h.

5.2.2.3 Meyer-Schuster Rearrangement.

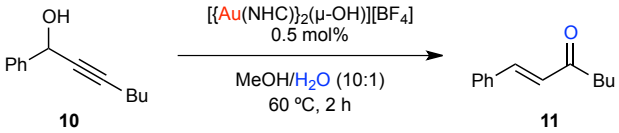
An alternative transformation for the synthesis of *α,β*-unsaturated ketones presented in Chapter 2 is the rearrangement of propargylic alcohols, known as the Meyer-Schuster rearrangement.[132] This reaction can be catalysed by acid or by several metal complexes.[132-133] The case of gold has been widely studied by several groups.[51,134] In 2009, our group reported that *α,β*-unsaturated ketones could be obtained in good yield by heating propargylic alcohols at 60 ºC for 16 h in a 10:1 mixture of MeOH/H_2O in the presence of 2 mol% of [Au(IPr)Cl]/$AgSbF_6$ (eq. 1, Scheme 6).[134d] Further investigations of this reaction allowed our group to report, one year later, the use of the Meyer-Schuster rearrangement for the synthesis of prostaglandins.[51b] Using 2 mol% of gold hydroxide **1a** (acid activated) or digold complex **2a**, in a 10:1 mixture of MeOH/H_2O, *α,β*-unsaturated ketones were obtained in very good to excellent conversions at room temperature (eq. 2, Scheme 6).[51b]



Scheme 6. Previous work done on gold-catalysed Meyer-Schuster rearrangement

The catalyst screening was carried out using propargylic alcohol **10** as substrate, as it has become our benchmark compound for the Meyer-Schuster rearrangement, and the latest set of conditions reported by our group.[51b] Initial results using 1 mol% and 0.5 mol% of digold complex **2a** allowed us to obtain 99% and 69% conversion, respectively, to the desired *α,β*-unsaturated ketone **11** in 3 h at room temperature. In order to use the lowest amount of catalyst combined with the shortest reaction times possible, experiments were conducted using 0.5 mol% of our diaurated complexes at 60 ºC for 2 h (Table 3). Unfortunately, under these conditions complexes **2c**-**2e** showed poor reactivity for this transformation, resulting in conversions between 3%-27% (Table 3, entries 3-5,). In the case of **2d**, this may be due to its poor solubility in the reaction mixture. On the other hand, the complexes bearing SIPr (**2b**) and IPr (**2a**) ligands showed good reactivity with excellent conversions (85 and 98% respectively; Table 3, entries 1 and 2). In order to test the limit of the system, a reaction was performed with 0.1 mol% of **2a** during 24 h. Satisfactorily, a good conversion (74%) was obtained (Table 3, entry 6). These results place the digold catalyst **2a** among the best for the gold-catalysed Meyer-Schuster rearrangement.

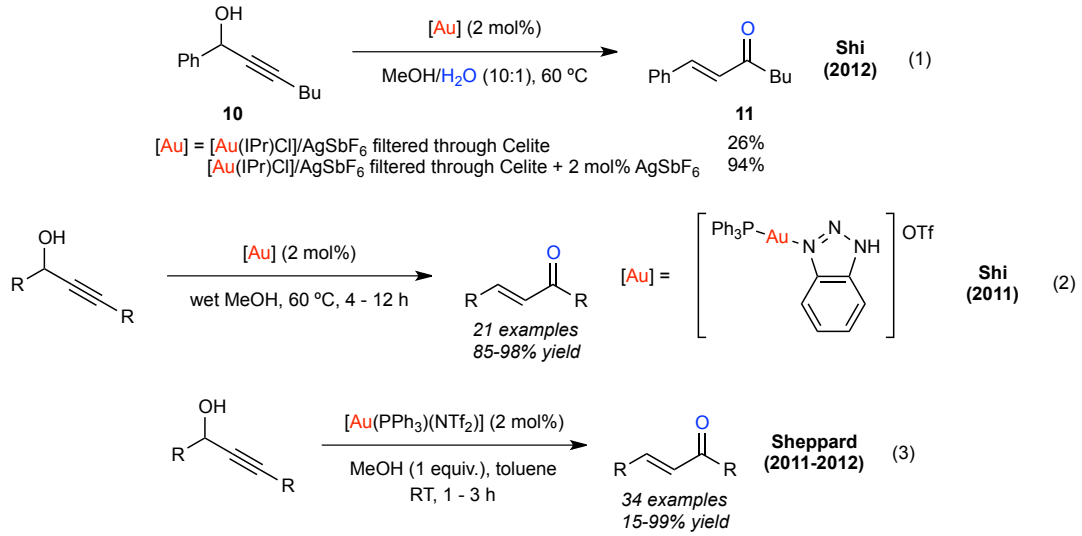
Table 3. Gold-catalysed Meyer-Schuster Rearrangement[a]



Entry	Catalyst	Conversion (%)[b]
1	**2a** [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (0.5)	98 (95)
2	**2b** [{Au(SIPr)}$_2$(μ-OH)][BF$_4$] (0.5)	85
3	**2c** [{Au(IPr^{Cl})}$_2$(μ-OH)][BF$_4$] (0.5)	18
4	**2d** [{Au(IPr*)}$_2$(μ-OH)][BF$_4$] (0.5)	3
5	**2e** [{Au(IPent)}$_2$(μ-OH)][BF$_4$] (0.5)	27
6[c]	**2a** [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (0.1)	74

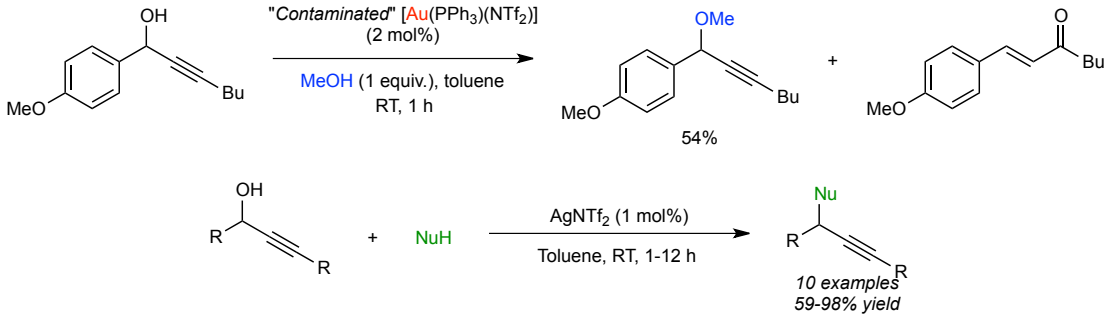
[a] Reaction conditions: [Au] (1 μmol), **10** (0.2 mmol) in a mixture of methanol/H$_2$O (10:1, 1 mL), 60 ºC, 2 h. [b] Conversions determined by GC. Average of at least 2 runs. Isolated yield in parentheses. [c] Reaction conditions: [Au] (1 μmol), **10** (1.0 mmol) in a mixture of methanol/H$_2$O (10:1, 1 mL), 60 ºC, 24 h.

Once again, our results contradict the conclusions of Shi and co-workers.[15] In their manuscript, they classify this transformation as an example of silver assisted gold-catalysed process. They described that this reaction can only be poorly catalysed by [Au(IPr)][SbF_6] (26% conversion), and that the addition of silver salts greatly enhanced the reactivity (94% conversion) (eq. 1, Scheme 7). Our results, in accordance with those published by Sheppard[134f,134h] and Shi himself (eq. 2-3, Scheme 7),[134g] highlight that *gold alone* can catalyse the Meyer-Schuster rearrangement in high yields.



Scheme 7. Silver free gold-catalysed Meyer-Schuster rearrangement

Interestingly, Sheppard also noticed that the presence of silver impurities in the gold catalyst afforded the substitution of the alcohol by the MeOH employed during the reaction.[134h] An exhaustive study of the reaction revealed that $AgNTf_2$ could catalyse this process and lead to the development of a silver-catalysed substitution reaction of propargylic alcohols (Scheme 8).[134h]

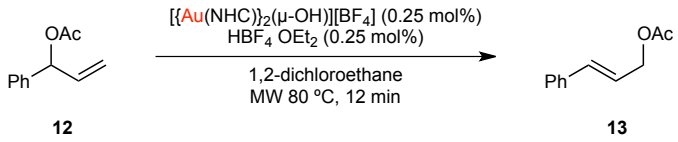


Scheme 8. Side reaction catalysed by $AgNTf_2$ impurities in the gold catalyst

5.2.2.4 Rearrangement of Allylic Acetates.

Finally, the rearrangement of allylic acetates was tested in order to study the potential of the new complexes as acid activated precatalysts. This classical skeletal rearrangement has been described as catalysed by several transition metals including gold.[97,135] As mentioned in Chapter 2, our group reported in 2007 the complete conversion of allylic acetate **12** into **13** after 12 min at 80 ºC in 1,2-dichloroethane using microwave irradiation and a combination of [Au(IPr)Cl] (3 mol%) and $AgBF_4$ (2 mol%).[97] More recently, we described the use of 1 mol% of [{Au(IPr)}$_2$(μ-OH)][BF_4]/HBF_4 under the same conditions during 30 min to obtain full conversion of **12** into **13**.[29] To determine the lowest amount of catalyst while maintaining shorter reaction times, reactions were carried out using 0.5 mol% of digold hydroxides **2a-e**, at 80 ºC in a microwave reactor (Table 4). Under these conditions, diaurated complexes **2a**, **2d** and **2e** provided moderate conversions, 59-67% (Table 4, entries 1, 4 and 5). Gratifyingly, the use of the SIPr and IPr^{Cl} derivatives, **2b** and **2c**, gave excellent conversions, 94-99% (Table 4, entries 2 and 3). In order to determine which was the most active catalyst, one more reaction was performed under the same conditions but at lower catalyst loading (0.1 mol%). We were very pleased to observe that even at these low loadings catalyst **2b** provided very high yields (90%).

Table 4. Gold-catalysed Allylic Acetate Rearrangement[a]



12 **13**

Entry	Catalyst (mol%)	Conversion (%)[b]
1	**2a** [{Au(IPr)}$_2$(μ-OH)][BF_4] (0.25)	63
2	**2b** [{Au(SIPr)}$_2$(μ-OH)][BF_4] (0.25)	99
3	**2c** [{Au(IPrCl)}$_2$(μ-OH)][BF_4] (0.25)	94
4	**2d** [{Au(IPr*)}$_2$(μ-OH)][BF_4] (0.25)	59
5	**2e** [{Au(IPent)}$_2$(μ-OH)][BF_4] (0.25)	67
6[c]	**2b** [{Au(SIPr)}$_2$(μ-OH)][BF_4] (0.1)	99 (90)
7[c]	**2c** [{Au(IPrCl)}$_2$(μ-OH)][BF_4] (0.1)	52

[a] Reaction conditions: [Au] (0.75 μmol), HBF_4•OEt_2 (0.75 μmol), **12** (0.3 mmol), in DCE (3 mL), 80 ºC, 12 min. [b] Conversions determined by GC. Average of at least 2 runs. Isolated yield in parentheses. [c] Reaction conditions: [Au] (0.3 μmol), HBF_4•OEt_2 (0.3 μmol), **12** (0.3 mmol), in DCE (3 mL), 80 ºC, 12 min.

5.3 Conclusion

In conclusion, three novel digold complexes have been synthesised and their catalytic activity tested in important organic transformations. Gratifyingly, very good results, over 90% isolated yields, were obtained at relatively low catalyst loadings (0.05-0.5 mol%) in the

reactions examined. Moreover, these digold catalysts do not require any additive (e.g. acid, silver salts) to promote water-inclusive reactions, such as alkyne and nitrile hydration and Meyer-Schuster rearrangement. In addition, digold hydroxides have shown to be suitable precatalyst, when activated by equimolar amounts of acid, for the rearrangement of allylic acetates. Particularly interesting are the results for the hydration of diphenylacetylene and the Meyer-Schuster rearrangement as they are in direct contradiction with some recent literature reports that claim that these reactions cannot be catalysed only by gold.

5.4 Experimental Section

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. Deuterated solvents (CD_2Cl_2, $CDCl_3$) were filtered through basic alumina in order to remove traces of HCl. NMR spectra were recorded on 300 and 400 MHz spectrometers at room temperature in CD_2Cl_2 or $CDCl_3$. Chemical shifts are given in parts per million (ppm) with respect to TMS. Elemental analyses were carried out by the analytical services of London Metropolitan University. [{Au(IPr)}$_2$(μ-OH)][BF_4] (**2a**) and [{Au(SIPr)}$_2$(μ-OH)][BF_4] (**2b**) were synthesised according to our previous reports (See Chapter 4 for more information).[29,31a,123] Diphenylacetylene and 4-methoxybenzonitrile were purchased from Alfa Aesar. Propargylic alcohol **10**[96] and allylic acetate **12**[97] were synthesised according to literature procedures.

General procedure for the synthesis of [{Au(NHC)}$_2$(μ-OH)][BF_4] ***2c-e***: To a solution of the corresponding [Au(NHC)Cl] (1 equiv.) in dry acetonitrile (5 mL), under an argon atmosphere, $AgBF_4$ (1.1 equiv.) was added. The reaction was stirred at room temperature, in the absence of light, for 5 h. The reaction mixture was then filtered through a pad of Celite®, the solvent removed *in vaccuo* and the crude dissolved in *ca.* 10 mL of CH_2Cl_2. The organic solution was washed three times with *ca*. 30 mL of distilled water, dried over anhydrous $MgSO_4$ and concentrated under vacuum.[136] To purify the final product two scenarios are possible: a) the resulting solid was dissolved in the minimum amount of CH_2Cl_2 (*ca.* 2 mL) and the product was precipitated by addition of pentane (*ca.* 8 mL) or b) if after evaporation of the solvent an oil is remaining the final product can be precipitated by addition of Et_2O (*ca.* 4 mL). The precipitate was collected by filtration, affording the desired complexes as white solids.

*[{Au(IPr^{Cl})}$_2$(μ-OH)][BF_4] (**2c**)*: Following the general procedure [Au(IPr^{Cl})Cl] (300 mg, 0.434 mmol) and $AgBF_4$ (93 mg, 0.478 mmol) were used. **2c** was obtained as a white solid in 81% isolated yield (248 mg, 0.175 mmol). **^{1}H NMR** (CD_2Cl_2; 400 MHz): δ 7.59 (t, J = 7.8

Hz, 4H, CH_{Ar}), 7.32 (d, J = 7.8 Hz, 8H, CH_{Ar}), 2.29 (sept, J = 6.9 Hz, 8H, C$H_{i\text{Pr}}$), 1.23 (d, J = 6.9 Hz, 24H, CH_3), 1.13 (d, J = 6.8 Hz, 24H, CH_3), 0.77 (s, 1H, OH). **^{13}C{^{1}H} NMR** (CD_2Cl_2; 101 MHz): δ 163.0 (C_{carb}), 146.4 (C_{Ar}), 132.2 (CH$_{Ar}$), 131.1 (C_{Ar}), 125.1 (CH$_{Ar}$), 120.1 (C_{Cl}), 29.4 (CH$_{i\text{Pr}}$), 24.8 (CH$_3$), 23.5 (CH$_3$). **^{19}F NMR** (CD_2Cl_2; 376 MHz): δ -153.89, -153.94. **Anal. Calcd.** for $C_{54}H_{69}Au_2BCl_4F_4N_4O$ (1412.70): C, 45.91; H, 4.92; N, 3.97. Found: C, 45.86; H, 4.83; N, 3.87.

[{Au(IPr)}$_2$(μ-OH)][BF_4] (**2d**)*: Following the general procedure [Au(IPr*)Cl] (300 mg, 0.262 mmol) and $AgBF_4$ (56 mg, 0.288 mmol) were used. **2d** was obtained as a white solid in 72% isolated yield (219.2 mg, 0.094 mmol). **^{1}H NMR** (300 MHz; CD_2Cl_2): δ 7.28-7.24 (m, 24H, CH_{Ar}), 7.06 (s, 8H, CH_{Ar}), 7.00-6.87 (m, 56H, CH_{Ar}), 5.98 (s, 4H, CH_{imid}), 5.24 (s, 8H, CHPh$_2$), 2.36 (s, 12H, CH_3), -0.76 (s, 1H, OH). **^{13}C{^{1}H} NMR** (75 MHz; CD_2Cl_2): δ 164.2 (C_{carb}), 142.85 (C_{Ar}), 142.68 (C_{Ar}), 141.3 (C_{Ar}), 140.9 (C_{Ar}), 134.0 (C_{Ar}), 131.0 (CH$_{Ar}$), 130.0 (CH$_{Ar}$), 129.6 (CH$_{Ar}$), 129.1 (CH$_{Ar}$), 128.8 (CH$_{Ar}$), 127.6 (CH$_{Ar}$), 127.1 (CH$_{Ar}$), 124.4 (CH$_{imid}$), 51.9 (CHPh$_2$), 22.1 (CH$_3$). **^{19}F NMR** (282 MHz; CD_2Cl_2): δ -153.96, -154.02. **Anal. Calcd.** for $C_{138}H_{113}Au_2BF_4N_4O$ (2324.14): C, 71.32; H, 4.90; N, 2.41. Found: C, 71.17; H, 4.77; N, 2.33.

*[{Au(IPent)}$_2$(μ-OH)][BF_4] (**2e**):* Following the general procedure [Au(IPr^{Cl})Cl] (300 mg, 0.409 mmol) and $AgBF_4$ (88 mg, 0.450 mmol) were used. **2e** was obtained as a white solid in 80% isolated yield (245.3 mg, 0.164). **^{1}H NMR** (CD_2Cl_2; 300 MHz): δ 7.53 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.20 (d, J = 7.8 Hz, 8H, CH_{Ar}), 7.07 (s, 4H, CH_{imid}), 1.97 (quintet, J = 7.1 Hz, 8H, CH), 1.66-1.37 (m, 32H, CH_2), 0.72 (dt, J = 12.9, 7.3 Hz, 48H, CH_3), 0.20 (s, 1H, OH). **^{13}C{^{1}H} NMR** (CD_2Cl_2; 75 MHz): δ 163.4 (C_{carb}), 143.7 (C_{Ar}), 136.8 (C_{Ar}), 130.8 (CH$_{Ar}$), 125.1 (CH$_{Ar}$), 124.8 (CH$_{imid}$), 43.2 (CH), 29.5 (CH$_2$), 28.6 (CH$_2$), 13.2 (CH$_3$), 12.6 (CH$_3$). **^{19}F NMR** (CD_2Cl_2; 282 MHz): δ -153.94, -154.00. **Anal. Calcd.** for $C_{70}H_{105}Au_2BF_4N_4O$ (1499.35): C, 56.07; H, 7.06; N, 3.74. Found: C, 55.89; H 7.12; N, 3.84.

Typical procedure for the alkyne hydration (Table 1, Entry 8): A solution of diphenylacetylene (446 mg, 5.0 mmol) in a 2:1 mixture of 1,4-dioxane/water (5 mL) was added to a solution of [{Au(IPr^{Cl})}$_2$(μ-OH)][BF_4] (1.8 mg, 2.5 μmol) in a 2:1 mixture of 1,4-dioxane/water (5 mL). The reaction mixture was stirred at 120 ºC for 24 h. Then it was diluted with EtOAc, and the aqueous layer extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous Mg2SO4. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 10/1) to give 1,2-diphenylethanone (439 mg, 90%) as a white solid whose NMR data matched the

literature.[137] **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 8.05-7.99 (m, 2H), 7.60-7.52 (m, 1H), 7.50-7.43 (m, 2H), 7.37-7.24 (m, 5H), 4.29 (s, 2H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz): δ 197.7, 136.7, 134.7, 133.3, 129.6, 128.78, 128.76, 128.73, 127.0, 45.6.

Typical procedure for the nitrile hydration (Table 2, Entry 2): [{Au(SIPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 2.5 mmol) was added to a solution of 4-methoxybenzonitrile (67 mg, 0.5 mmol) in a 1:1 mixture of THF/water (1 mL). The reaction mixture was stirred at 140 ºC for 2 h in a scientific microwave reactor. Then it was diluted with EtOAc, and the aqueous layer extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous Mg_2SO_4. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 10/1 ~ EtOAc only) to give 4-methoxybenzamide (69 mg, 90%) as a white solid whose NMR data matched the literature.[130] **^{1}H NMR** (DMSO-d_6, 300 MHz): δ 7.90-7.78 (m, 1H), 7.18 (brs, 1H), 7.03-6.91 (m, 2H), 3.80 (s, 3H). **^{13}C{^{1}H} NMR** (DMSO-d_6, 75 MHz): δ 167.5, 161.6, 129.4, 126.5, 113.4, 55.3.

Typical procedure for Meyer-Schuster Rearrangement (Table 3, Entry 1): [{Au(IPr)}$_2$(μ-OH)][BF_4] (1.3 mg, 1.0 mmol) was added to a solution of 1-phenylhept-2-yn-1-ol (38 mg, 0.2 mmol) in a 10:1 mixture of MeOH/water (1 mL). The reaction mixture was stirred at 60 ºC for 2 h. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (hexane/ EtOAc = 10/1) to give (*E*)-1-phenylhept-1-en-3-one (36 mg, 90%) as a white solid whose NMR data matched the literature.[40] **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.61-7.51 (m, 3H), 7.45-7.36 (m, 3H), 7.75 (d, *J* = 16.2 Hz, 1H), 2.67 (t, *J* = 7.4 Hz, 2H), 1.64 (tt, *J* = 7.4, 7.4 Hz, 2H) 1.39 (tt, *J* = 7.4, 7.4 Hz, 1H 2H), 0.95 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz): δ 200.9, 142.5, 134.7, 130.5, 129.1, 128.4, 126.4, 40.8, 26.6, 22.6, 14.1.

Typical procedure for Allylic Acetate Rearrangements (Table 3, Entry 6): A (1/1000) solution of $HBF_4{\cdot}OEt_2$ in dichloromethane was added to a solution of [{Au(IPr)}$_2$(m-OH)][BF_4] (0.38 mg, 0.30 mmol) in dichloromethane (1 mL). The reaction mixture was stirred for 5 min at room temperature and a solution of allylic acetate (53 mg, 0.30 mmol) in 1,2-dichloroethane (1 mL) was added. The reaction mixture was stirred at 80 ºC for 30 min in a scientific microwave reactor. Pentane was added and the resulting solution was filtered through a pad of Celite. After removal of solvent, the residue was purified by flash column chromatography on silica gel (hexane/ EtOAc = 10/1) to give the product (48.2 mg, 91%) as a colorless oil whose NMR data matched the reported one.[97] **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.44-7.22 (m, 5H), 6.60 (dt, *J* = 15.9, 1.4 Hz, 1H), 6.29 (dt, *J* = 15.9, 6.5 Hz, 1H), 4.73 (dd, *J*

= 6.5, 1.4 Hz, 2H), 2.11 (s, 3H). **$^{13}C\{^1H\}$ NMR** ($CDCl_3$, 75 MHz): δ 171.0, 136.3, 124.3, 128.7, 128.2, 126.7, 123.3, 65.2, 21.2.

6. *gem*-Diaurated and Digold σ,π-Acetylide Species

6.1 Introduction

The advent of gold-mediated transformations has led to significant advances in organic synthesis.[2a,2c-e,2k,138] The majority of the synthetic/catalytic uses of gold catalysts rely on the well-documented ability of *monomeric* gold complexes to activate C-C multiple bonds or to form C-Au σ-bonds that can be further functionalised. In contrast, the chemistry of dinuclear gold complexes, recently highlighted,[53,139] remains relatively unexplored. Such complexes can activate organic molecules *via* the formation of either *gem*-diaurated or σ,π-activated alkyne complexes (Figure 1).

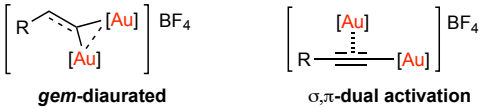
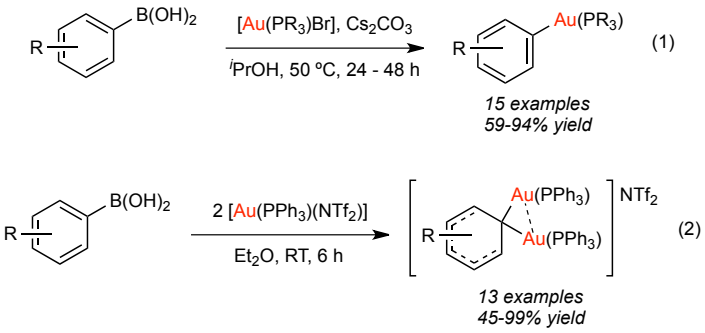


Figure 1. Example of *gem*-diaurated and σ,π-activated molecules

Formation of both types of dinuclear gold species during catalytic transformations is more common than first thought, especially in reactions involving terminal alkynes.[53-55,57,65] The number of publications highlighting these species is increasing as researchers become aware of their existence and actively attempt to identify them. Thus, a robust and reliable synthesis of key digold complexes is central to achieve these goals. Therefore, we sought to develop a straightforward methodology leading to *gem*-diaurated and σ,π-acetylide species to permit further synthetic and mechanistic studies.

Several groups have contributed significantly to the understanding of the reactivity of both *gem*-diaurated and σ,π-acetylide species (see Chapter 1 for more detailed information).[2g,52,60-61,140] While access to the latter class is relatively facile,[54-55] the formation of *gem*-diaurated compounds often involve tedious and/or circuitous procedures.[141] It was not until Gray developed a methodology to transmetalate aryl boronic acids with [Au(PPh_3)Br], using Cs_2CO_3 in *iso*-propanol to form mononuclear gold species, that a door to milder procedures was opened (eq. 1, Scheme 1).[142] Recently, his group has progressed one step further and extended this methodology to the synthesis of [{Au(PPh_3)}$_2$(μ-aryl)][NTf_2] species using 2 equiv. of Gagosz's complex [Au(PPh_3)(NTf_2)][22b] in dry diethyl ether at room temperature (eq. 2, Scheme 1).[63]



Scheme 1. Synthesis of mono- and di-aurated species reported by Gray and co-workers

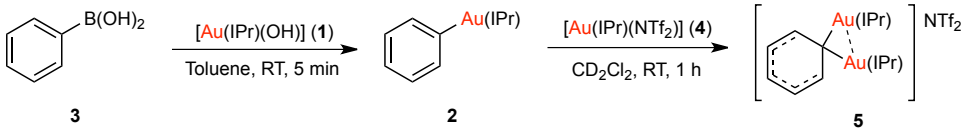
In this context, and despite the vast utility of *N*-heterocyclic carbene (NHC) ligands in homogenous catalysis[4] in general and in Au-catalysis in particular,[5a,118c] only a handful of examples of *gem*-diaurated-NHC species are known.[64b,64d,64e] These species were synthesised by first isolating a vinyl/aryl-gold complex and then reacting it with 1 equiv. of a suitable gold species, such as [Au(NHC)NTf_2].[64b,64d,64e] Therefore, in order to be able to study this type of species in detail and get a better understanding of their properties and reactivity, the development of a more straightforward methodology leading to the synthesis of *gem*-diaurated-NHC species would be highly desirable.

6.2 Results and Discussion

6.2.1 *gem-Diaurated Species*

6.2.1.1 Synthesis and Characterisation

We recently reported the synthesis of mononuclear organogold complexes (**2**) bearing NHC ligands in a rapid and efficient manner *via* transmetallation from boronic acids using a gold hydroxide species, [Au(IPr)(OH)] (**1**).[49] We thought that if we initially formed [Au(IPr)(Ph)] (**2**) by reacting **1** with phenyl boronic acid (**3**), the addition of Gagosz's complex [Au(IPr)(NTf_2)][22a] (**4**) should form the *gem*-diaurated species [{Au(IPr)}$_2$(μ-phenyl)][NTf_2] (**5**). As hypothesised, **5** was obtained in quantitative conversion after 1 h at room temperature (Scheme 2).

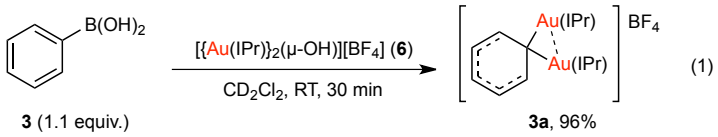


Scheme 2. Synthesis of diaurated species **5** using the **1** and Gagosz's complex **4**.

As explained in Chapter 1, digold hydroxide species can be seen as a combination of [Au(OH)] + $[Au]^+$. Therefore, encouraged by the result of the sequential reaction, we

envisioned a general one-step procedure leading to *gem*-diaurated complexes using a digold hydroxide complex, such as [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (**6**) as synthon.[29,31a,143]

Initial reaction of **6** (1 equiv.) with phenylboronic acid **3** (1 equiv.) in CD_2Cl_2 at room temperature resulted in complete conversion of the starting materials and disappearance of the characteristic μ-OH signal (~0.4 ppm)[29] of **6** within 30 min (eq. 1). The product was precipitated by the addition of pentane, collected by filtration and dried under vacuum affording a white powder in 96% yield.



(1)

Further characterisation of the product by $^{13}C\{^1H\}$ NMR spectroscopy, elemental analysis and single crystal X-ray diffraction studies confirmed the formation of [{Au(IPr)}$_2$(μ-phenyl)][BF$_4$] (**3a**) (left, Figure 2).

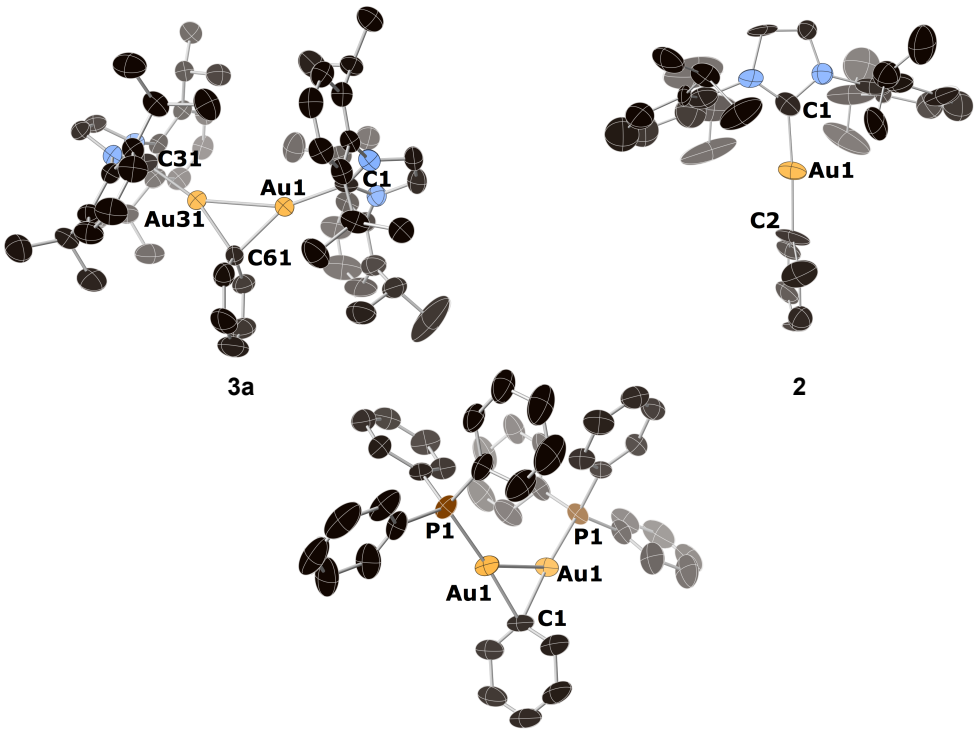
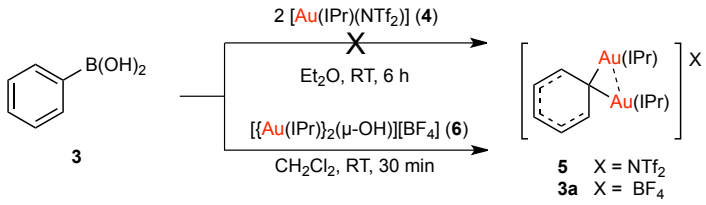


Figure 2. Molecular structures of **3a** (left), **2** (right) and [{Au(PPh$_3$)}$_2$(μ-phenyl)][NTf$_2$]. H atoms, and counterions are omitted for clarity. Selected bond distances (Å) and angles (°) for **3a**: Au1-C1 2.017(8), Au1-C61 2.141(8), Au1-Au31 2.7697(8), Au31-C31 2.007(8), Au31-C61 2.122(8), Au31-Au1-C1 154.8(2), Au31-Au1-C61 49.2(2), C1-Au1-C61 155.6(3), Au1-Au31-C31 148.9(3) and C31-Au31-C61 160.6(3); for **2** (range between 3 independent molecules): Au-C1 2.00(3)-2.06(3), Au-C2 2.01(3)-2.09(3) and C1-Au-C2 172.9(13)-178.1(11); and for [{Au(PPh$_3$)}$_2$(μ-phenyl)][NTf$_2$]: P1-Au1-C1 175.70(8), Au1-Au1 2.7112(6), P1-Au1 2.2617(10) and C1-Au1 2.153(4).

In contrast to the monoaurated complex [Au(IPr)(Ph)] (**2**) (right, Figure 2), diaurated species **3a** does not adopt the classical linear conformation for Au^{I}-complexes and presents C_{carb}-Au-C_{phenyl} angles of 155.6(3)º and 160.6(3)º. Most likely, this non-linearity is due to the strong aurophilic interaction between the two gold centres and the steric hindrance of the carbene ligands. The Au-Au distance, 2.7697(8) Å, falls in the range of those reported in the literature (2.727-2.846 Å).[64d] While the C_{carb}-Au bond lengths are almost the same in **2** and **3a**, the C_{phenyl}-Au bond lengths are slightly longer in **3a**. This is in agreement with the more cationic nature of **3a** and the "three-center-two-electron" system in the Au-C_{carb}-Au bond. If **3a** is compared to its phosphane congener [{Au(PPh_3)}$_2$(μ-phenyl)][NTf_2], reported by Gray,[63] significant differences can be noted (middle, Figure 2). The latter presents the typical linear conformation for Au^{1}-complexes with a P-Au-C_{phenyl} angle of 175.70(8)º and a shorter Au-Au distance of 2.7112(6) Å. As expected, the P-Au bond (2.2617(10) Å) is longer that the C_{carb}-Au bond length. On the other hand, the C_{phenyl}-Au length is slightly longer for the phosphine complex (2.153(4) Å) than for **3a**.

6.2.1.2 Optimisation Studies

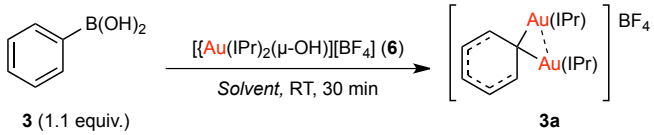
In order to compare the methodology reported by Gray[63] to the present route, the reaction between 2 equiv. of Gagosz's complex **4** and boronic acid **3** under both sets of conditions was carried out. No conversion to the desired product was observed when **4** was used, but the use of **6** under our initial conditions appears to be a very general protocol (Scheme 3).



Scheme 3. Comparison between Gray's methodology and the one developed in this work.

Encouraged by these results, we proceeded to optimise the initial reaction conditions. Six different solvents were tested: 1,4-dioxane, THF, toluene, CH_2Cl_2, Et_2O and 2-methyltetrahydrofuran (Table 1). No dramatic effect was observed and all the reactions afforded full conversion to **3a** by ^{1}H NMR spectroscopy, and the isolated yields were between 80-97%. The best solvents, affording 97 and 96% isolated yields of **3a** were toluene and CH_2Cl_2, respectively. For practical reasons, the latter was selected as the optimal solvent.

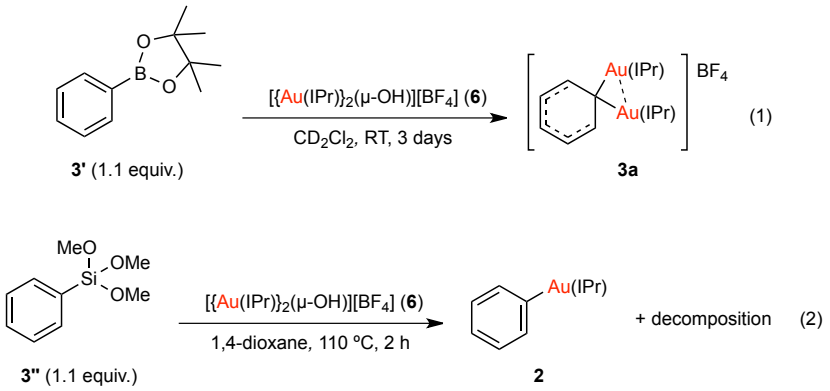
Table 1. Solvent optimisation[a]



Entry	Solvent	^{1}H NMR conversion (%)	Isolated Yield (%)
1	1,4-dioxane	> 99	89
2	THF	> 99	80
3	Toluene	> 99	97
4	CH_2Cl_2	> 99	96
5	Et_2O	> 99	89
6	2-methyltetrahydrofuran	> 99	80

[a] Reaction conditions: **6** (15.7 μmol), **3** (17.3 μmol, 1.1 equiv.), solvent (0.5 mL), RT, 1 h.

Different organometallic partners were also screened (Scheme 4). The use of phenylboronic acid pinacol ester (**3'**) resulted in significantly slower transmetallation and three days were necessary to reach full conversion (eq. 1, Scheme 4). Following our group's recent contribution on the transmetallation between $RSi(OMe)_3$ and **1**,[50] we attempted to employ siloxanes to access *gem*-diaurated species. Reaction of siloxane **3''** and digold-hydroxide **6**, in 1,4-dioxane at 110 ºC, afforded the monoaurated complex **2** as the main product (eq. 2, Scheme 4). The formation of a black precipitate and a gold mirror was also observed. We suspect that this may be due to the high temperatures required for the reaction to proceed.



Scheme 4. Screening of potential coupling partners

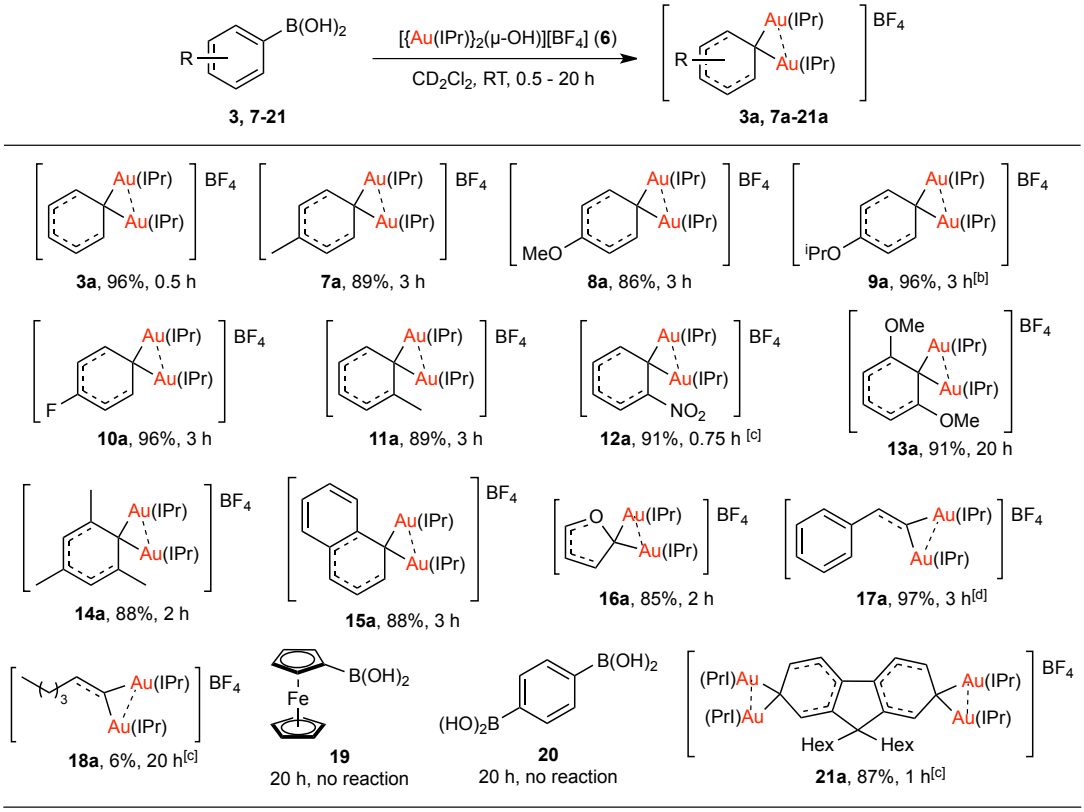
6.2.1.3 Substrate Scope

With the optimisation results in hand, we proceeded to explore the substrate scope and limitations of the method (Table 1). Generally, 1.1 equiv. of boronic acid was sufficient to reach completion within a few hours. Most reactions afforded the desired product in excellent yields and various functionalities were tolerated, e.g. methoxy, fluoro and nitro groups.

Phenylboronic acids with either electron-withdrawing (EWG) or electron-donating (EDG) groups at the *para*-position required increased reaction times compared to **3** (**7a-10a**, Table 1). Interestingly, reaction with *para-iso*-propoxyphenylboronic acid (**9**) afforded the desired product **9a** in excellent yield, although 2 equiv. of boronic acid were necessary to allow reaction completion (**9a**, Table 1). This result is a great improvement from previous literature reports that disclosed a 45% yield.[63] Surprisingly, a dramatic electronic effect was observed when EWG or EDG occupied the *ortho*-position to the reactive centre. While the use of EDG resulted in the need for longer reaction times (**13a**, Table 1), the *ortho*-nitro substituent reduced this time to 45 min (**12a**, Table 1).[144] The dramatically longer reaction times observed for 2,6-dimethoxyphenylboronic acid (**13**) could be explained by the electron-donating ability of the methoxy groups and the high steric congestion about the substrate reactive site.

More challenging architectures were then targeted. The use of 2-furanboronic acid (**16**) afforded the expected product in excellent yield after 2 h (**16a**, Table 1). Access to vinyl-*gem*-diaurated species was also investigated. Reactions with the *trans*-styreneboronic acid (**17**) needed 1.5 equiv. of boronic acid to reach completion, but afforded the desired product in 97% yield (**17a**, Table 1). As observed by Fürstner, this type of *gem*-diaurated species easily undergoes decomposition in CD_2Cl_2.[61b] Unfortunately, attempts to extend this methodology to other vinylboronic acids, such as **18**, were unsuccessful, irrespective of the number of equivalents of starting material used (**18a**, Table 1). In contrast, reaction of 2 equiv. of the ferrocene derivative **19** with **6** afforded only the mononuclear gold complex, while reaction with only 1 equiv. resulted in no conversion (**19**, Table 1). The synthesis of bis-*gem*-diaurated species was also attempted. While the reaction with bis-boronic acid **20** did not afford any product, regardless of the reaction times or number of equivalents of boronic acid used, reaction with **21** showed a 87% conversion to the desired product within 1 h (**21a**, Table 2). Unfortunately, attempts to force the reaction to completion or to separate **21a** from **6** were unsuccessful.

Table 1. Scope using boronic acids[a]



[a] Reaction conditions: **6** (20 mg, 15.7 μmol), boronic acid (1.1 equiv.), CH_2Cl_2 (0.5 mL), RT. [b] **9** (2 equiv.). [c] Conversion as determined by ^{1}H NMR spectroscopy. [d] **17** (1.5 equiv.).

All compounds isolated in Table 1 were characterised by ^{1}H NMR, ^{13}C{^{1}H} NMR and yielded correct elemental analyses. It is worthwhile noting that previous phosphane analogues were reported without ^{13}C{^{1}H} NMR spectra of the complexes because attempts to identify the bridging *ipso*-carbon were unsuccessful.[63] Very careful investigation of the carbene system using long delays and a large number of scans allowed us to identify the *ipso*-carbon by NMR spectroscopy for almost all products. In order to confidently assign structural features, HSQC and HMBC experiments were necessary. The chemical shifts for these *ipso*-carbons appear between 106.5 (**13a**) and 148.4 (**15a**) ppm for the phenyl derivatives, 158.2 for **16a** and 122.6 for the vinyl species **17a**. It was possible to grow suitable crystals for single crystal X-ray diffraction (XRD) studies for compounds **7a, 9a, 10a, 13a, 15a** and **17a** by slow diffusion of pentane into a saturated solution of the product in THF at 4 ºC (Figure 3). Unfortunately, the quality of the crystals does not allow comment on the structural features (bond lengths, angles) of the aforementioned complexes.

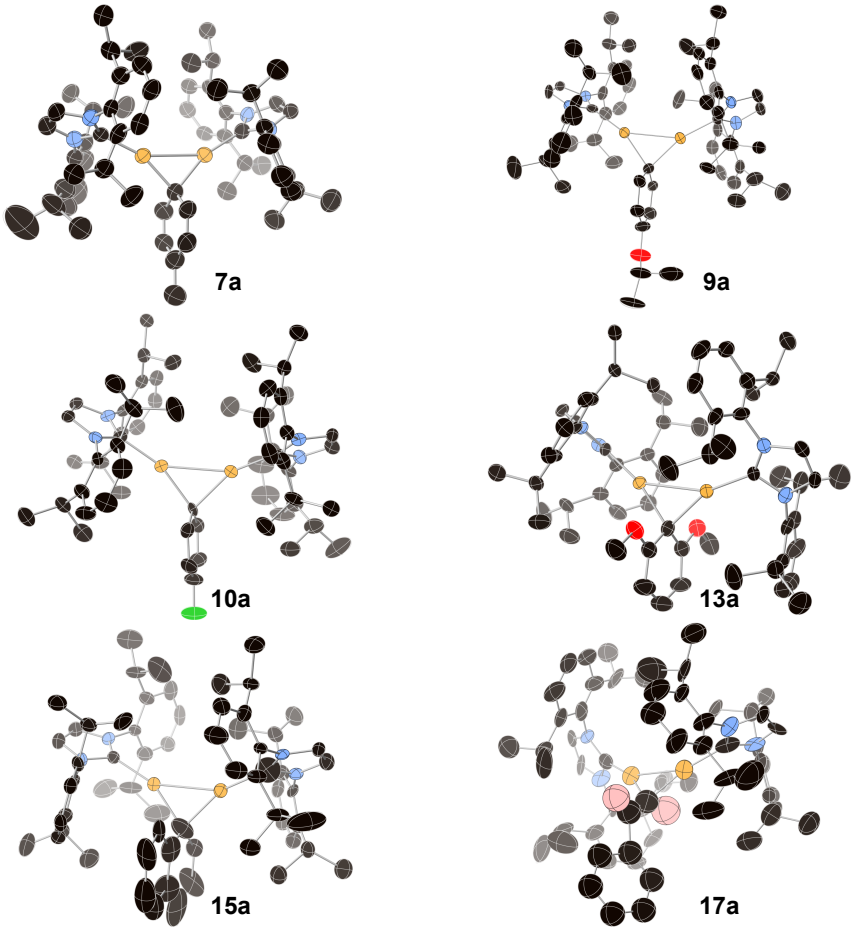
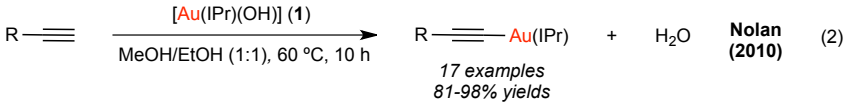


Figure 3. Structural confirmation of species **7a**, **9a**, **10a**, **13a**, **15a and 17a**. Most H atoms and all the counterions are omitted for clarity.

6.2.2 *Diaurated σ,π-Acetylide Species: Synthesis and Characterisation*

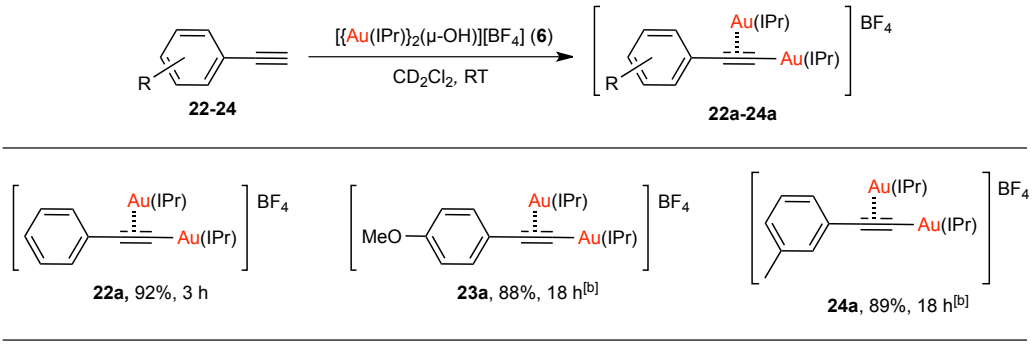
Once the effectiveness of our method for the synthesis of *gem*-diaurated species was demonstrated, we wondered if the methodology could be extended to the synthesis of digold σ,π-acetylide species, thereby further extending the use of **6** as a synthon. For alternative routes for the synthesis of this type of species see Chapter 1. Previous studies from our group showed that Au-OH **1** can react with terminal alkynes to form gold-acetylide species in a simple and straightforward manner producing only water as a side product (eq. 2).[43]



Since digold hydroxide **6** can be seen as a combination of [Au(OH)] + $[Au]^+$ we envision that its reaction with terminal alkynes would result in the straightforward formation of diaurated σ,π-acetylide species with water as the sole side product of the reaction. Initial reaction of phenylacetylene (**22**) with **6** in CH_2Cl_2 at room temperature afforded the desired

diaurated σ,π-acetylide species **22a** in excellent yield within 3 h (**22a**, Table 3). The diaurated nature of compound **22a** was confirmed by XRD (Figure 4) as well as by comparison of the ^{1}H and $^{13}C\{^{1}H\}$ NMR data with that reported by Widenhoefer.[54] The reaction was then attempted with two additional substrates. These results are summarised in Table 3. All three complexes were obtained in excellent yields and both *para* and *meta*-electron-donating substituents were tolerated (**23a** and **24a**, Table 3).

Table 3. Synthesis of σ,π-acetylide species[a]



[a] Reaction conditions: **6** (20 mg, 15.7 μmol, 1 equiv.), alkyne (1 equiv.), CH_2Cl_2 (0.5 mL), rt. [b] Reaction times are not optimised.

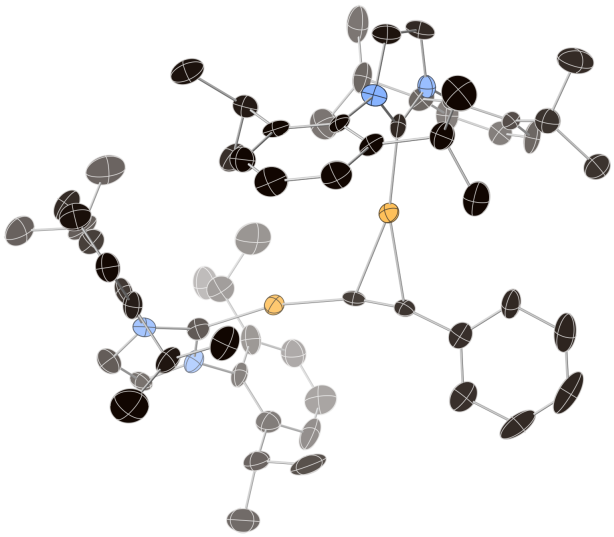


Figure 3. Molecular structure of **22a**. H atoms and counterion are omitted for clarity.

6.3 Conclusion

In conclusion we have developed a new, mild and straightforward methodology for the synthesis of *gem*-diaurated-NHC species in excellent yields using $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ (**6**). This new synthetic protocol proves to be highly efficient for a wide range of phenyl derivatives bearing EWG, EDG and sterically demanding substituents, as well as for

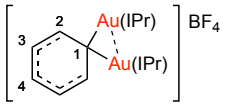
heteroaromatic species. This procedure fulfils the need for highly efficient methodologies for the synthesis of *gem*-diaurated-NHC complexes. In addition, **6** could also be used to gain access to σ,π-acetylide species. We hope that this methodology will help in mechanistic studies to elucidate the role of dinuclear gold species in the on-going *"Gold Rush*".

6.4 Experimental Section

Unless otherwise stated, all boronic acids and terminal alkynes were used as purchased and all reactions were performed under air. Chlorinated solvents (CH_2Cl_2 and CD_2Cl_2) were filtered through basic alumina in order to remove traces of HCl. NMR spectra were recorded on 500, 400 and 300 MHz spectrometers at room temperature in CD_2Cl_2. The specific number of scans (Ns) and delay times (d1) used in order to determine the bridging *ipso*-carbon (C^1) in each $^{13}C\{^1H\}$ NMR experiment are provided in the experimental details. Elemental analyses were carried out by the analytical services of London Metropolitan University. CCDC 905570 (**2**), 905571 (**3a**), 905572 (**7a**), 905573 (**9a**), 905574 (**10a**), 905575 (**13a**), 905576 (**15a**), 905577 (**17a**) and 905578 (**22a**) contain the supplementary crystallographic data for this Chapter. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre (CCDC) via http://www.ccdc.cam.ac.uk/data_request/cif.

*General procedure for the Synthesis of [{Au(IPr)}$_2$(μ-aryl)][BF$_4$] species (**3a, 7a-21a**)*: Digold hydroxide complex **6** (20 mg, 15.7 μmol, 1 equiv.) and the corresponding boronic acid (from 1.1 to 2 equiv.) were dissolved in CH_2Cl_2 (0.5 mL) and stirred at room temperature between 0.5-24 h. Afterwards, the product was precipitated by addition of pentane (2 mL) and some drops of diethyl ether (if needed), filtered, washed with pentane and dried under vacuum.

*[{Au(IPr)}$_2$(μ-phenyl)][BF$_4$] (**3a**)*: Following the general procedure, using 1.1 equiv. of



phenylboronic acid. Complex **3a** was recovered as a white powder in 96% isolated yield (20.1 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.48 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.18 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 7.16 (s, 4H, C*H*$_{imid}$), 7.02-6.98 (m, 1H, C*H*^{4}), 6.81-6.77 (m, 2H, C*H*^{3}), 6.38 (dd, *J* = 7.8, 1.3 Hz, 2H, C*H*^{2}), 2.31 (sept, *J* = 6.8 Hz, 8H, C*H*$_{iPr}$), 1.09 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 0.83 (d, *J* = 6.9 Hz, 24H, C*H*$_3$). **^{13}C{^{1}H} NMR** (101 MHz, Ns = 800, d1 = 5 sec; CD_2Cl_2): δ 184.9 (*C*$_{Carb}$), 147.2 (*C*H^2), 145.8 (*C*$_{Ar}$), 136.1 (*C*^{1}), 134.0 (*C*$_{Ar}$), 133.7 (*C*H^4), 130.9 (*C*H$_{Ar}$), 127.4 (*C*H^3), 124.4 (*C*H$_{Ar}$), 124.0 (*C*H$_{imid}$), 28.9 (*C*H$_{iPr}$), 24.15 (*C*H$_3$), 24.03 (*C*H$_3$). **^{19}F NMR** (376 MHz, CD_2Cl_2): δ -153.92, -153.97. **Anal. Calc.** for $C_{60}H_{77}Au_2BF_4N_4$ (1335.02): C, 53.98; H, 5.81; N, 4.20. Found C, 53.88, H, 5.89, N, 4.32.

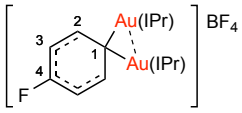
*[{Au(IPr)}$_2${μ-(4-methylphenyl)}][BF$_4$] (**7a**)*: Following the general procedure, using 1.1 equiv. of 4-methylphenylboronic acid. Complex **7a** was recovered as a white powder in 89% isolated yield (18.8 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.48 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.18 (d, *J* = 7.9 Hz, 8H, C*H*$_{Ar}$), 7.15 (s, 4H, C*H*$_{imid}$), 6.61 (d, *J* = 7.4 Hz, 2H, C*H*^{3}), 6.29 (d, *J* = 8.0 Hz, 2H, C*H*^{2}), 2.31 (sept, *J* = 6.9 Hz, 8H, C*H*$_{iPr}$), 2.21 (s, 3H, C*H*$_3^5$), 1.09 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 0.83 (d, *J* = 6.9 Hz, 24H, C*H*$_3$). **^{13}C{^{1}H} NMR** (101 MHz, Ns = 800, d1 = 5 sec; CD_2Cl_2): δ 185.2 (*C*$_{Carb}$), 147.3 (*C*H^2), 145.8 (*C*$_{Ar}$), 144.7 (*C*^{4}), 134.1 (*C*$_{Ar}$), 131.1 (*C*^{1}), 130.8 (*C*H$_{Ar}$), 128.4 (*C*H^3), 124.4 (*C*H$_{Ar}$), 124.0 (*C*H$_{imid}$), 28.9 (*C*H$_{iPr}$), 24.13 (*C*H$_3$), 24.03 (*C*H$_3$), 21.6 (*C*H$_3^5$). **^{19}F NMR** (376 MHz, CD_2Cl_2): δ -153.93, -153.98. **Anal. Calc.** for $C_{61}H_{79}Au_2BF_4N_4$ (1349.05): C, 54.31; H, 5.90; N, 4.15. Found C, 54.19, H, 5.82, N, 4.27.

*[{Au(IPr)}$_2${μ-(4-methoxyphenyl)}][BF$_4$] (**8a**)*: Following the general procedure, 1.1 equiv. of 4-methoxyphenylboronic acid were used. Complex **8a** was recovered as a white powder in 86% isolated yield (18.4 mg). **^{1}H NMR** (500 MHz; CD_2Cl_2): δ 7.48 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.18 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 7.14 (s, 4H, C*H*$_{imid}$), 6.36 (q, *J* = 6.9 Hz, 4H, C*H*^{2,3}), 3.69 (s, 3H, OC*H*$_3$), 2.32 (sept, *J* = 6.9 Hz, 8H, C*H*$_{iPr}$), 1.09 (d, *J* = 6.9 Hz, 24H, *C*H$_3$), 0.84 (d, *J* = 6.9 Hz, 24H, *C*H$_3$). **^{13}C{^{1}H} NMR** (75 MHz, Ns = 2400, d1 = 1.5 sec; CD_2Cl_2): δ 185.5 (*C*$_{Carb}$), 164.9 (*C*^{4}), 149.4 (*C*H^2), 145.8 (*C*$_{Ar}$), 134.2 (*C*$_{Ar}$), 130.8 (*C*H$_{Ar}$), 124.6 (*C*^{1}), 124.4 (*C*H$_{Ar}$), 124.0 (*C*H$_{imid}$), 113.9 (*C*H^3), 55.5 (O*C*H$_3$), 28.9 (*C*H$_{iPr}$), 24.18 (*C*H$_3$), 24.06 (*C*H$_3$). **^{19}F NMR** (282 MHz; CD_2Cl_2): δ -154.04, -154.10. **Anal. Calc.** for $C_{61}H_{79}Au_2BF_4N_4O$ (1365.04): C, 53.67; H, 5.83; N, 4.10. Found C, 53.51, H, 5.81, N, 4.14.

*[{Au(IPr)}$_2${μ-(4-(iso-propoxy)phenyl)}][BF$_4$] (**9a**)*: Following the general procedure, using 2 equiv. of 4-*iso*-propoxyphenylboronic acid. Complex **9a** was recovered as a white powder in 96% isolated yield (20.9 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.48 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.18 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 7.14 (s, 4H, C*H*$_{imid}$), 6.36-6.30 (m, 4H, C*H*^{2,3}), 4.44 (sept, *J* = 6.1 Hz, 1H, OC*H*(CH$_3$)$_2$), 2.32 (sept, *J* = 6.8 Hz, 8H, C*H*$_{iPr}$), 1.25 (d, *J* = 6.1 Hz, 6H, OCH(C*H*$_3$)$_2$), 1.09 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 0.84 (d, *J* = 6.9 Hz, 24H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz, Ns = 2400, d1 = 1.5 sec; CD_2Cl_2): δ 185.7 (*C*$_{Carb}$), 163.4 (*C*^{4}), 149.5 (*C*H^2), 145.8 (*C*$_{Ar}$), 134.2 (*C*$_{Ar}$), 130.8 (*C*H$_{Ar}$), 124.8 (*C*H$_{Ar}$), 124.4 (*C*H$_{imid}$), 123.9 (*C*^{1}), 115.3 (*C*H^3), 69.9 (O*C*H(CH$_3$)$_2$), 28.9 (*C*H$_{iPr}$), 24.17 (*C*H$_3$), 24.05 (*C*H$_3$), 21.9 (OCH(*C*H$_3$)$_2$). **^{19}F NMR** (282

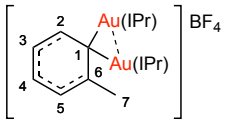
MHz; CD_2Cl_2): δ -153.93, -153.98. **Anal. Calc.** for $C_{63}H_{83}Au_2BF_4N_4O$ (1393.10): C, 54.32; H, 6.01; N, 4.02. Found C, 54.17, H, 5.92, N, 3.92.

*[{Au(IPr)}$_2${μ-(4-fluorophenyl)}][BF_4] (**10a**)*: Following the general procedure, using 1.1



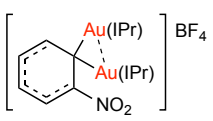
equiv. of 4-fluorophenylboronic acid. Complex **10a** was recovered as a white powder in 86% isolated yield (18.3 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.49 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.19 (d, J = 7.8 Hz, 8H, CH_{Ar}), 7.18 (s, 4H, CH_{imid}), 6.57-6.53 (m, 2H, CH^3), 6.42-6.38 (m, 2H, CH^2), 2.31 (sept, J = 6.9 Hz, 8H, C$H_{i\text{Pr}}$), 1.10 (d, J = 6.9 Hz, 24H, CH_3), 0.84 (d, J = 6.9 Hz, 24H, CH_3). **^{13}C{^{1}H} NMR** (126 MHz, Ns = 2400, d1 = 2 sec; CD_2Cl_2): δ 184.3 (C_{Carb}), 167.1 (d, $J_{C\text{-}F}$ = 254.4 Hz, CF^4), 149.1 (d, $J_{C\text{-}F}$ = 7.9 Hz, CH^2), 145.8 (C_{Ar}), 134.0 (C_{Ar}), 131.2 (C^1), 130.9 (CH_{Ar}), 124.4 (CH_{Ar}), 124.1 (CH_{imid}), 115.0 (d, $J_{C\text{-}F}$ = 20.0 Hz, CH^3), 28.9 ($CH_{i\text{Pr}}$), 24.2 (CH_3), 24.0 (CH_3). **^{19}F{^{1}H} NMR** (376 MHz; CD_2Cl_2): δ -105.5, -153.91, -153.96. **Anal. Calc.** for $C_{60}H_{76}Au_2BF_5N_4$ (1353.01): C, 53.26; H, 5.66; N, 4.14. Found C, 53.36, H, 5.77, N, 4.25.

*[{Au(IPr)}$_2${μ-(2-methylphenyl)}][BF_4] (**11a**)*: Following the general procedure, using 1.1



equiv. of 2-methylphenylboronic acid. Complex **11a** was recovered as a white powder in 89% isolated yield (18.8 mg). **^{1}H NMR** (300 MHz; CD_2Cl_2): δ 7.49 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.20 (ddd, J = 11.9, 7.8, 1.3 Hz, 8H, CH_{Ar}), 7.15 (s, 4H, CH_{imid}), 6.93 (td, J = 7.5, 1.4 Hz, 1H, CH^3), 6.79 (dd, J = 7.6, 0.4 Hz, 1H, CH^5), 6.70-6.65 (m, 1H, CH^4), 6.50 (dd, J = 7.4, 1.3 Hz, 1H, CH^2), 2.40 (m, 4H, C$H_{i\text{Pr}}$), 2.32-2.19 (m, 4H, C$H_{i\text{Pr}}$), 1.08 (dd, J = 6.9, 1.8 Hz, 24H, CH_3), 0.99 (s, 3H, CH_3^7), 0.95 (d, J = 6.9 Hz, 12H, CH_3), 0.72 (d, J = 6.9 Hz, 12H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, Ns = 1600, d1 = 5 sec; CD_2Cl_2): δ 184.9 (C_{Carb}), 158.4 (C^6), 148.4 (CH^2), 145.86 (C_{Ar}), 145.73 (C_{Ar}), 137.1 (C^1), 134.3 (C_{Ar}), 133.4 (CH^3), 130.9 (CH_{Ar}), 127.3 (CH^5), 124.53 (CH_{Ar}), 124.47 (CH_{Ar}), 124.1 ($CH_{imidazole}$), 123.9 (CH^4), 29.01 ($CH_{i\text{Pr}}$), 28.95 ($CH_{i\text{Pr}}$), 26.6 (CH_3^7) 24.28 (CH_3), 24.15 (CH_3), 24.02 (CH_3), 23.95 (CH_3). **^{19}F NMR** (282 MHz; CD_2Cl_2): δ -154.01, -154.06. **Anal. Calc.** for $C_{61}H_{79}Au_2BF_4N_4$ (1349.05): C, 54.31; H, 5.90; N, 4.15. Found C, 54.21, H, 5.78, N, 4.22.

*[{Au(IPr)}$_2${μ-(2-nitrophenyl)}][BF_4] (**12a**)*: Following the general procedure, using 1



equiv. of 2-nitrophenylboronic acid. Complex **12a** was recovered as a white powder in 91% isolated yield (19.6 mg). **^{1}H NMR** (300 MHz; CD_2Cl_2): δ 7.97 (dd, J = 8.2, 1.1 Hz, 1H, C$H_{p\text{-}NO_2}$), 7.49 (t, J = 7.8 Hz, 4H), 7.35 (d, J = 7.8 Hz, 1H, C$H_{p\text{-}NO_2}$), 7.23-7.10 (m, 13H, CH_{Ar} + CH_{imid} + C$H_{p\text{-}NO_2}$), 6.58 (dd, J = 7.2, 1.4 Hz, 1H, C$H_{p\text{-}NO_2}$), 2.37-2.19 (m, 8H, C$H_{i\text{Pr}}$), 1.07 (d, J = 6.9 Hz, 24H, CH_3),

0.90 (d, J = 6.9 Hz, 12H, CH_3), 0.73 (d, J = 6.9 Hz, 12H, CH_3). ^{13}C NMR and elemental analysis could not be recorded for **13b** due to rapid decomposition of the diaurated complex to the monoaurated aryl species and the cationic species [Au(IPr)][BF_4].

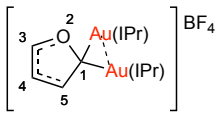
*[{Au(IPr)}$_2${μ-(2,6-dimethoxyphenyl)}][BF_4] (**13a**)*: Following the general procedure, using 1.1 equiv. of 2,6-dimethoxyphenylboronic acid. Complex **13a** was recovered as a white powder in 91% isolated yield (19.8 mg). **^{1}H NMR** (300 MHz; CD_2Cl_2): δ 7.46 (t, J = 7.9 Hz, 4H, CH_{Ar}), 7.17 (d, J = 7.8 Hz, 8H, CH_{Ar}), 7.10 (s, 4H, CH_{imid}), 6.95 (t, J = 8.1 Hz, 1H, CH^4), 6.01 (d, J = 8.1 Hz, 2H, CH^3), 2.90 (s, 6H, OCH_3), 2.33 (sept, J = 6.9 Hz, 8H, C$H_{i\text{Pr}}$), 1.08 (d, J = 6.9 Hz, 24H, CH_3), 0.88 (d, J = 6.9 Hz, 24H, CH_3). **^{13}C{^{1}H} NMR** (75 MHz; Ns = 1600, d1 = 5 sec, CD_2Cl_2): δ 184.2 (C_{Carb}), 176.1 (C^2), 145.9 (C_{Ar}), 137.5 (CH^4), 134.4 (C_{Ar}), 130.6 (CH_{Ar}), 124.3 (CH_{Ar}), 123.9 (CH_{imid}), 106.5 (C^1), 101.7 (CH^3), 55.0 (OCH_3), 29.0 ($CH_{i\text{Pr}}$), 24.12 (CH_3), 23.99 (CH_3). **^{19}F NMR** (282 MHz; CD_2Cl_2): δ -153.91, -153.98. **Anal. Calc.** for $C_{62}H_{81}Au_2BF_4N_4O_2$ (1395.07): C, 53.38; H, 5.85; N, 4.02. Found C, 53.26, H, 5.79, N, 4.09.

*[{Au(IPr)}$_2${μ-(2,4,6-trimethylphenyl)}][BF_4] (**14a**):* Following the general procedure, using 1.3 equiv. of 2,4,6-trimetheylphenylboronic acid. Complex **14a** was recovered as a white powder in 88% isolated yield (19.1 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.47 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.20 (d, J = 7.8 Hz, 8H, CH_{Ar}), 7.14 (s, 4H, CH_{imid}), 6.46 (s, 2H, CH^3), 2.32 (sept, J = 6.8 Hz, 8H, C$H_{i\text{Pr}}$), 2.16 (s, 3H, CH_3^5), 1.07 (d, J = 6.9 Hz, 24H, CH_3), 1.02 (s, 6H, CH_3^6), 0.87 (d, J = 6.9 Hz, 24H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz, Ns = 1600, d1 = 5 sec; CD_2Cl_2): δ 185.0 (C_{Carb}), 159.5 (C^2), 145.8 (C_{Ar}), 144.9 (C^4), 134.6 (C_{Ar}), 133.8 (C^1), 130.8 (CH_{Ar}), 125.7 (CH^2), 124.5 (CH_{Ar}), 124.1 (CH_{imid}), 29.0 ($CH_{i\text{Pr}}$), 26.9 (CH_3^6), 24.4 (CH_3), 23.9 (CH_3), 21.2 (CH_3^5). **^{19}F NMR** (376 MHz; CD_2Cl_2): δ -153.97, -154.02. **Anal. Calc.** for $C_{63}H_{83}Au_2BF_4N_4$ (1377.10): C, 54.95; H, 6.08; N, 4.07. Found C, 54.94, H, 6.11, N, 4.14.

*[{Au(IPr)}$_2${μ-(1-naphatalene)}][BF_4] (**15a**):* Following the general procedure, using 1.1 equiv. of 1-naphthaleneboronic acid. Complex **15a** was recovered as a white powder in 88% isolated yield (19.1 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.57 (d, J = 8.2 Hz, 2H, C$H^{5,6}$), 7.44 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.28 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H, CH^9), 7.18 (dd, J = 7.8, 1.3 Hz, 4H, CH_{Ar}), 7.12 (s, 4H, CH_{imid}), 7.05 (dd, J = 7.8, 1.3 Hz, 4H, CH_{Ar}), 6.92 (dd, J = 8.1, 6.9 Hz, 1H, CH^8), 6.85 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H, CH^4), 6.78 (dd, J = 6.7, 1.1 Hz, 1H, CH^{10}), 6.53 (d, J = 8.2 Hz, 1H, CH^3), 2.30 (sept, J = 6.9 Hz, 4H, C$H_{i\text{Pr}}$), 2.20 (sept, J = 6.8

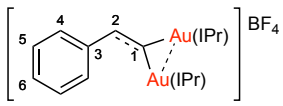
Hz, 4H, C$H_{i\mathrm{Pr}}$), 1.06 (d, J = 6.9 Hz, 12H, CH_3), 1.01 (d, J = 6.9 Hz, 12H, CH_3), 0.84 (d, J = 6.9 Hz, 12H, CH_3), 0.56 (d, J = 6.9 Hz, 12H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz, Ns = 1600, d1 = 5 sec; CD_2Cl_2): δ 184.6 (C_{Carb}), 148.4 (C^1), 146.7 (CH^{10}), 145.69 (C_{Ar}), 145.58 (C_{Ar}), 138.2 (C^2), 134.1 (C_{Ar}), 133.2 (CH^5), 132.8 (C^7), 132.0 (CH^3), 130.9 (CH_{Ar}), 127.8 (CH^6), 126.5 (CH^4), 125.9 (CH^9), 124.43 (CH_{Ar}), 124.36 (CH_{Ar}), 124.31 (CH^8), 124.0 (CH_{imid}), 28.89 ($CH_{i\mathrm{Pr}}$), 28.86 ($CH_{i\mathrm{Pr}}$), 24.16 (CH_3), 24.10 (CH_3), 24.04 (CH_3), 23.7 (CH_3). **^{19}F NMR** (376 MHz; CD_2Cl_2): δ -153.97, -154.02. **Anal. Calc.** for $C_{64}H_{79}Au_2BF_4N_4$ (1385.08): C, 55.50; H, 5.75; N, 4.05. Found C, 55.36, H, 5.70, N, 4.12.

*[{Au(IPr)}$_2${μ-(2-furan)}][BF$_4$] (**16a**):* Following the general procedure, using 2 equiv. of



2-furanboronic acid. Complex **16a** was recovered as a white powder in 85% isolated yield (17.6 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.53 (d, J = 1.6 Hz, 1H, CH^3), 7.49 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.22-7.18 (m, 8H, CH_{Ar}), 7.16 (s, 4H, CH_{imid}), 6.41 (d, J = 3.4 Hz, 1H, CH^5), 6.15 (dd, J = 3.4, 1.6 Hz, 1H, CH^4), 2.34 (sept, J = 6.8 Hz, 8H, C$H_{i\mathrm{Pr}}$), 1.11 (dd, J = 6.9, 2.3 Hz, 24H, CH_3), 0.91 (d, J = 6.9 Hz, 12H, CH_3), 0.87 (d, J = 6.9 Hz, 12H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz, Ns = 800, d1 = 5 sec; CD_2Cl_2): δ 183.5 (C_{Carb}), 158.7 (CH^3), 158.2 (C^1), 149.9 (CH^5), 145.87 (C_{Ar}), 145.71 (C_{Ar}), 134.0 (C_{Ar}), 130.9 (CH_{Ar}), 124.47 (CH_{Ar}), 124.46 (CH_{Ar}), 124.2 (CH_{imid}), 110.4 (CH^4), 28.98 ($CH_{i\mathrm{Pr}}$), 28.96 ($CH_{i\mathrm{Pr}}$), 24.29 (CH_3), 24.23 (CH_3), 24.06 (CH_3), 23.92 (CH_3). **^{19}F NMR** (376 MHz; CD_2Cl_2): δ -153.93, -153.98. **Anal. Calc.** for $C_{58}H_{75}Au_2BF_4N_4O$ (1324.98): C, 52.58; H, 5.71; N, 4.23. Found C, 52.40, H, 5.78, N, 4.31.

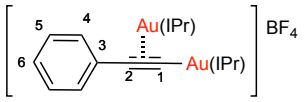
*[{Au(IPr)}$_2${μ-(trans-styrene)}][BF$_4$] (**17a**):* Following the general procedure, 1.5 equiv.



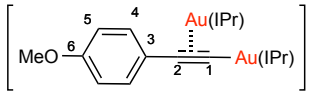
of *trans*-β-styreneboronic acid were used. Complex **17a** was recovered as a white powder in 97% isolated yield (20.7 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.45 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.27-7.22 (m, 3H, H^5 + H^6), 7.22-7.20 (d, J = 7.7 Hz , 4H, CH_{Ar}), 7.16 (s 4H, CH_{imid}), 7.15 (signal partially overlapped with the one of CH_{imid}, d, J = 7.7 Hz, 4H, CH_{Ar}), 6.86-6.84 (m, 2H, CH^4), 6.16 (d, J = 18.5 Hz, 1H, H^2), 5.83 (d, J = 18.4 Hz, 1H, H^1), 2.41-2.34 (m, 8H, C$H_{i\mathrm{Pr}}$), 1.11 (dd, J = 6.7, 5.2 Hz, 24H, CH_3), 0.97 (d, J = 6.9 Hz, 12H, CH_3), 0.91 (d, J = 6.9 Hz, 12H, CH_3). **^{13}C{^{1}H} NMR** (126 MHz, Ns = 2400, d1 = 2 sec; CD_2Cl_2): δ 185.0 (C_{Carb}), 168.5(CH^2), 145.85 (C_{Ar}), 145.73 (C_{Ar}), 135.8 (C^3), 134.0 (C_{Ar}), 130.9 (CH_{Ar}), 130.5 (CH^6), 128.4 (CH^5), 127.8 (CH^4), 124.5 (CH_{Ar}), 124.1 (CH_{imid}), 122.6 (CH^1), 28.98 ($CH_{i\mathrm{Pr}}$), 28.95 ($CH_{i\mathrm{Pr}}$), 24.40 (CH_3), 24.26 (CH_3), 24.02 (CH_3), 23.94 (CH_3). **^{19}F NMR** (282 MHz; CD_2Cl_2): δ -153.90, -153.96. **Anal. Calc.** for $C_{62}H_{79}Au_2BF_4N_4$ (1361.06): C, 54.71; H, 5.85; N, 4.12. Found C, 54.72, H, 5.91, N, 4.14.

General procedure for the Synthesis of [{Au(IPr)}$_2$(η^1, η^2-acetylide)][BF$_4$] species ***(22a-24a)***: Digold hydroxide complex **6** (1 equiv.) was added to a solution of the corresponding alkyne (1 equiv.) in CH_2Cl_2 (0.5 mL) at room temperature between 3-18 h. Afterwards, the product was precipitated by addition of pentane, filtered, washed with pentane and dried under vacuum.

[{Au(IPr)}$_2$(η^1, η^2-phenylacetylene)][BF$_4$] ***(23a)***: Following the general procedure, 1 equiv. of phenylacetylene (4.5 mg, 44 mmol) and 1 equiv. of **6** (56.1 mg, 44 mmol). Complex **23a** was recovered as an off-white powder in 92% isolated yield (55.6 mg). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.52 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.26 (d, *J* = 7.9 Hz, 8H, C*H*$_{Ar}$), 7.24 (s, 4H, C*H*$_{imid}$), 7.22 (m, 1H, C*H*^{6}), 7.08 (m, 2H, C*H*^{4}), 6.69 (m, 2H, C*H*^{5}), 2.45 (sept, *J* = 6.9 Hz, 8H, C*H*$_{iPr}$), 1.17 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 1.07 (d, *J* = 6.9 Hz, 24H, C*H*$_3$). **^{13}C{^{1}H} NMR** (75 MHz; CD_2Cl_2): δ 182.8 (*C*$_{Carb}$), 145.9 (*C*$_{Ar}$), 134.0 (*C*$_{Ar}$), 132.1 (*C*H^4), 131.2 (*C*H$_{Ar}$), 129.9 (*C*H^6), 128.7 (*C*H^5), 124.6 (*C*H$_{Ar}$), 124.5 (*C*H$_{imid}$), 124.3 (*C*^{1}), 120.9 (*C*^{3}), 112.8 (*C*^{2}), 29.1 (*C*H$_{iPr}$), 24.6 (*C*H$_3$), 24.1 (*C*H$_3$). **^{19}F NMR** (282 MHz; CD_2Cl_2): δ -153.43, -153.51. **Anal. Calc**. for $C_{63}H_{80}Au_2BF_4N_4$ (1374.07): C, 55.07; H, 5.87; N, 4.08. Found C, 55.02, H, 5.80, N, 4.09.



[{Au(IPr)}$_2${η^1, η^2-(4-methoxyphenylacetylene)}][BF$_4$] ***(24a)***: Following the general procedure, 1 equiv. of 4-methoxyphenylacetylene (2 mg, 15.7 mmol) and 1 equiv. of **6** (20 mg, 15.7 mmol). Complex **24a** was recovered as a yellow powder in 88% isolated yield (19.4 mg). **^{1}H NMR** (500 MHz; CD_2Cl_2): δ 7.51 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.26 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 7.22 (s, 4H, C*H*$_{imid}$), 6.66 (d, *J* = 8.8 Hz, 2H, C*H*^{5}), 6.60 (d, *J* = 8.8 Hz, 2H, C*H*^{4}), 3.76 (s, 3H, OC*H*$_3$), 2.43 (sept, *J* = 6.9 Hz, 8H, C*H*$_{iPr}$), 1.16 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 1.06 (d, *J* = 6.9 Hz, 24H, C*H*$_3$). **^{13}C{^{1}H} NMR** (126 MHz; CD_2Cl_2): δ 182.9 (*C*$_{Carb}$), 161.1 (*C*^{6}), 145.9 (*C*$_{Ar}$), 134.14 (*C*H^5), 133.98 (*C*$_{Ar}$), 131.1 (*C*H$_{Ar}$), 125.4 (*C*^{1}), 124.6 (*C*H$_{Ar}$), 124.4 (*C*H$_{imid}$), 121.0 (*C*^{3}), 114.3 (*C*H^4), 112.6 (*C*^{2}), 55.7 (O*C*H$_3$), 29.1 (*C*H$_{iPr}$), 24.6 (*C*H$_3$), 24.1 (*C*H$_3$). **^{19}F NMR** (471 MHz; CD_2Cl_2): δ -153.46, -153.52. **Anal. Calc.** for $C_{64}H_{82}Au_2BF_4N_4O$ (1404.10): C, 54.75; H, 5.89; N, 3.99. Found C, 54.64, H, 5.78, N, 4.05.



[{Au(IPr)}$_2${η^1, η^2-(2-methylphenylacetylene)}][BF$_4$] ***(25a)***: Following the general procedure, 1 equiv. of 4-methoxyphenylacetylene (2 mg, 15.7 mmol) and 1 equiv. of **6** (20 mg, 15.7 mmol). Complex **25a** was recovered as a yellow powder in 88% isolated yield (19.4 mg). **^{1}H NMR** (500 MHz; CD_2Cl_2): δ 7.51 (t, *J* = 7.8 Hz, 4H, C*H*$_{Ar}$), 7.26 (d, *J* = 7.8 Hz, 8H, C*H*$_{Ar}$), 7.23 (s, 4H, C*H*$_{imid}$), 7.05-7.03 (m, 1H, C*H*^{6}), 6.96 (t, *J* = 7.6 Hz, 1H, C*H*^{5}), 6.68 (s, 1H, C*H*^{9}), 6.48 (d, *J* = 7.7 Hz, 1H, C*H*^{4}), 2.44 (7, *J* = 6.9 Hz, 8H, C*H*$_{i\text{Pr}}$), 2.17 (s, 3H, C*H*$_3^8$), 1.17 (d, *J* = 6.9 Hz, 24H, C*H*$_3$), 1.07 (d, *J* = 6.9 Hz, 24H, C*H*$_3$). **^{13}C{^{1}H} NMR** (126 MHz; CD_2Cl_2): δ 182.9 (*C*$_{Carb}$), 145.9 (C$_{Ar}$), 138.5 (C^7), 133.9 (C$_{Ar}$), 132.8 (*C*H^9), 131.1 (*C*H$_{Ar}$), 130.9 (*C*H^6), 129.3 (*C*H^4), 128.6 (*C*H^5), 124.59 (*C*H$_{Ar}$), 124.45 (*C*H$_{imidazole}$), 123.7 (*C*^{1}), 120.7 (*C*^{3}), 113.1 (*C*^{2}), 29.1 (*C*H$_{i\text{Pr}}$), 24.6 (*C*H$_3$), 24.1 (*C*H$_3$), 21.2 (*C*H$_3^8$). **^{19}F NMR** (471 MHz; CD_2Cl_2): δ -153.46, -153.51. **Anal. Calc.** for $C_{64}H_{82}Au_2BF_4N_4$ (1388.10): C, 55.38; H, 5.95; N, 4.04. Found C, 55.27, H, 5.88, N, 4.06.

7. Hydrophenoxylation of Alkynes *via* Cooperative Gold Catalysis

7.1 Introduction

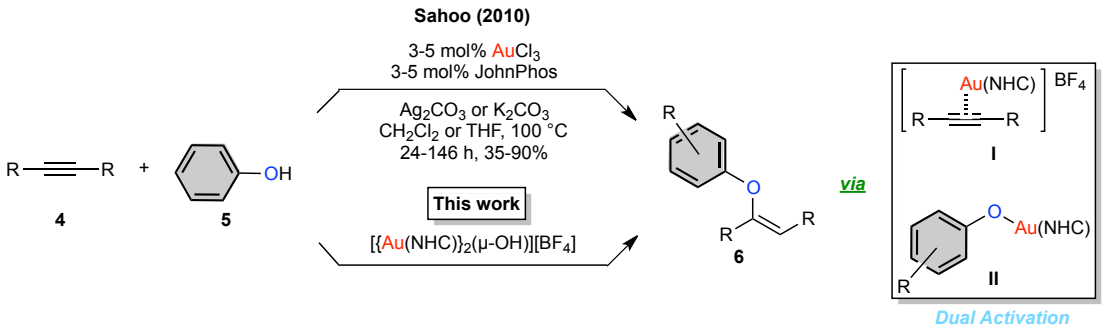
Over the past decade, the concept of cooperative or dual catalysis has emerged as an attractive and effective strategy to access unique reactivity and selectivity in synthetic organic chemistry.[145] This type of catalysis has been shown in dual organo-catalysed,[146] organo- and transition-metal-catalysed,[147] homobimetallic transition-metal-catalysed[148] and heterobimetallic- catalysed[149] processes. Recently, it has also received increased attention in gold chemistry due to the synthesis and isolation of dinuclear organogold species, such as *gem*-diaurated or σ,π-diaurated-acetylide complexes (see Chapter 1 for more details).[139] These species were first proposed and later identified as key intermediates or catalyst reservoirs in gold-catalysed reactions.[52,60,61b,64c-e,64g,65] Our group has recently contributed to this field with the synthesis of dinuclear gold hydroxide species $[\{Au(NHC)\}_2(\mu\text{-}OH)][BF_4]$ (**1**) (NHC = *N*-heterocyclic carbene), which can be easily prepared from commercially available [Au(NHC)(X)] (X = OH or Cl) complexes (see Chapter 1 for more details).[29,31a] Complexes **1** have been shown to be highly active catalysts for silver-free gold-catalysed transformations (See Chapter 5 for more details).[31b] We have also recently reported straightforward routes to both *gem*-diaurated and σ,π-diaurated-acetylide species by reacting **1A** (NHC = IPr) with aryl/vinyl boronic acids and terminal alkynes, respectively (See Chapter 6 for more details).[150] In addition, complexes **1** exhibited particularly interesting catalytic properties. For example, during studies of the gold-catalysed nitrile hydration our group observed that the use of **1A** afforded higher conversions to the desired amide than the gold monomer $[Au(IPr)(NTf_2)]$.[31a] Our group has previously postulated that $[\{Au(NHC)\}_2(\mu\text{-}OH)][BF_4]$ (**1**) could be considered as a combination of $[Au(NHC)][BF_4]$ (**2**) and [Au(NHC)(OH)] (**3**).[29,31a] We believed that, under the appropriate reaction conditions, this equilibrium could be displaced thus liberating a Lewis acid **2** and a Brønsted base **3** that could produce a synergistic effect leading to enhanced catalytic activity (eq. 1).

$$\underset{\mathbf{1}}{[\{Au(NHC)\}_2(\mu\text{-}OH)][BF4]} \rightleftharpoons \underset{\mathbf{2}}{[Au(NHC)][BF_4]} + \underset{\mathbf{3}}{[Au(NHC)(OH)]} \quad (1)$$

Lewis acid — Brønsted base

Most gold-catalysed transformations take advantage of the well-documented ability of the gold centre to activate C-C multiple bonds, typically alkynes, towards nucleophilic attack.[2d,5,151] While the addition of primary and secondary alcohols to alkynes is relatively well known,[28,94,152] reports of the addition of tertiary alcohols and phenols remain scarce. To

the best of our knowledge, there is only one report dealing with the gold-catalysed hydrophenoxylation of alkynes.[153] In 2010, Sahoo described the reaction between internal alkynes **4** and phenols **5** (2 equiv.) using 3-5 mol% of $AuCl_3$ in the presence of K_2CO_3 or Ag_2CO_3 (2 equiv.) under very harsh reaction conditions.[153] We envisioned that if **1** could act as bifunctional catalysts, the cationic gold species **2** might react with **4** forming π-gold-alkyne complexes **I**[154] while gold hydroxide **3** might react with **5** forming a gold-phenoxide complexes **II**[44-45] (Scheme 1).

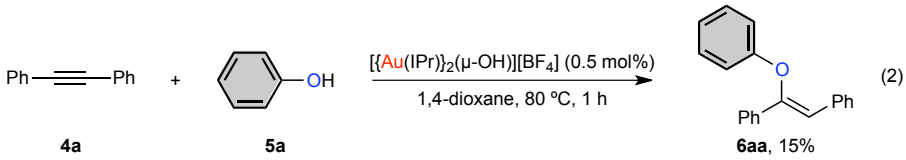


Scheme 1. Dual-activation in the hydrophenoxylation of alkynes.

7.2 Results and Discussion

7.2.1 *Optimisation Studies*

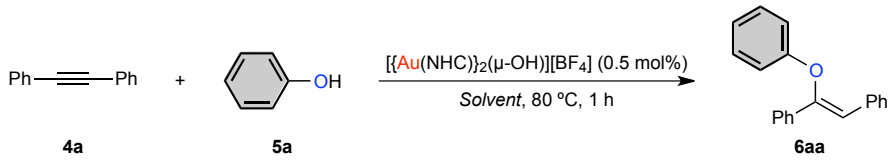
As a starting point we decided to use the reaction conditions that our group reported for the gold-catalysed alkyne hydration (see Chapter 5 for more information). Therefore, we began our studies by reacting diphenylacetylene **4a** and phenol **5a** (1.1 equiv.) in 1,4-dioxane at 80 ºC using **1A** (0.5 mol%) as catalyst. We were pleased to observe, after 1 h, an encouraging 15% conversion to the desired vinyl ether **6aa** by GC (eq. 2).



With this result in hand, we proceeded to optimise the reaction conditions (Table 1). Interestingly, the use of acetonitrile and DMF shut down the reaction (Entries 2 and 3, Table 1). On the other hand, 1,2-dichloroethane afforded good conversions (Entry, 4, Table 1). In toluene, 97% conversion was reached within 1 h at 80 ºC (Entry 5, Table 1). The ^{1}H NMR spectrum of the isolated product (96%) confirmed the stereospecific formation of *Z*-isomer **6aa**. Next, we screened various digold hydroxide complexes. While the catalyst bearing SIPr ligands performed poorly, IPr^{Cl} and IPent derivatives[31b,155] afforded good to excellent conversions (Table 1, entries 6-8). Since [{Au(IPr)}$_2$(μ-OH)][BF_4] afforded slightly better

conversions and can be easily synthesised from commercially available complexes, 0.5 mol% of **1A** in toluene at 80 ºC was selected as our optimised catalytic conditions. This new methodology affords a turn over frequency (TOF) of 4 orders of magnitude higher than the previous state-of-the-art (192 h^{-1} *vs.* 0.05 h^{-1}).[153]

Table 1. Optimisation of the reaction conditions.[a]



Entry	NHC	Solvent	Conversion (%)[b]
1	IPr	1,4-dioxane	15
2	IPr	CH_3CN	2
3	IPr	DMF	1
4	IPr	1,2-dichloroethane	75
5	IPr	toluene	97 (96)
6	SIPr	toluene	45
7	IPr^{Cl}	toluene	94
8	IPent	toluene	86

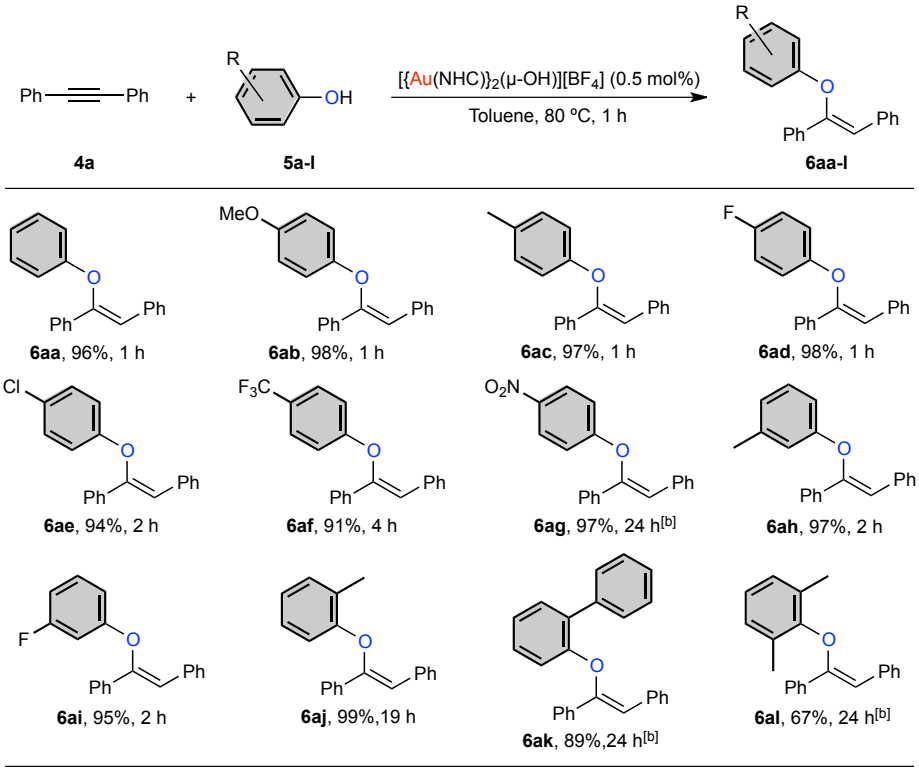
[a] Conditions: **4a** (0.50 mmol), **5a** (0.55 mmol, 1.1 equiv.), [Au] (0.5 mol%), solvent (1 mL), 80 °C. [b] Conversions determined by GC. Average of at least two runs. Isolated yield in parentheses.

7.2.2 *Substrate Scope*

Having established the optimised reaction conditions, the scope and limitations of the methodology were explored. We first examined the reaction between diphenylacetylene **4a** and several phenol derivatives (Table 2). The reaction of phenols **5b** and **5c**, bearing electron-donating groups at the *para*-position, proceeded smoothly to afford the desired aryl vinyl ethers **6ab** and **6ac** in high yields within 1 h (Table 2). In contrast, phenols **5d-5g** bearing electron-withdrawing groups at the *para*-position needed longer reaction times to reach completion. The corresponding compounds **6ad-6ag** were all isolated in high yields (91-98%). The reaction time increases as follows: MeO ~ Me ~ H ~ F < Cl < CF_3 < NO_2. Interestingly, this trend is the opposite of that observed by Sahoo,[153] which points to a different reaction mechanism operating in these two systems. In Sahoo's case,[153] as his protocol requires stoichiometric amounts of base the reactivity is dictated by the acidity of the phenol derivative; more acidic phenols, *i.e.* those bearing EWG, react faster. While, in our case, the nucleophilicity of the Au-phenoxide species dictates the reactivity, thus more nucleophilic phenoxides, i.e. those bearing EDG, react faster. The use of sterically hindered substrates was then tested. The reaction with *ortho*-substituted phenols (**5j** and **5k**) afforded the expected ethers (**6aj** and **6ak**) in 99% and 89% yields respectively, although at a cost of longer reaction times. Surprisingly, even the use of the highly sterically hindered 2,6-

dimethylphenol (**5l**), which was completely unreactive in Sahoo's study,[153] afforded the desired product **6al** in 67% yield.

Table 2. Hydrophenoxylation using various phenols.[a]

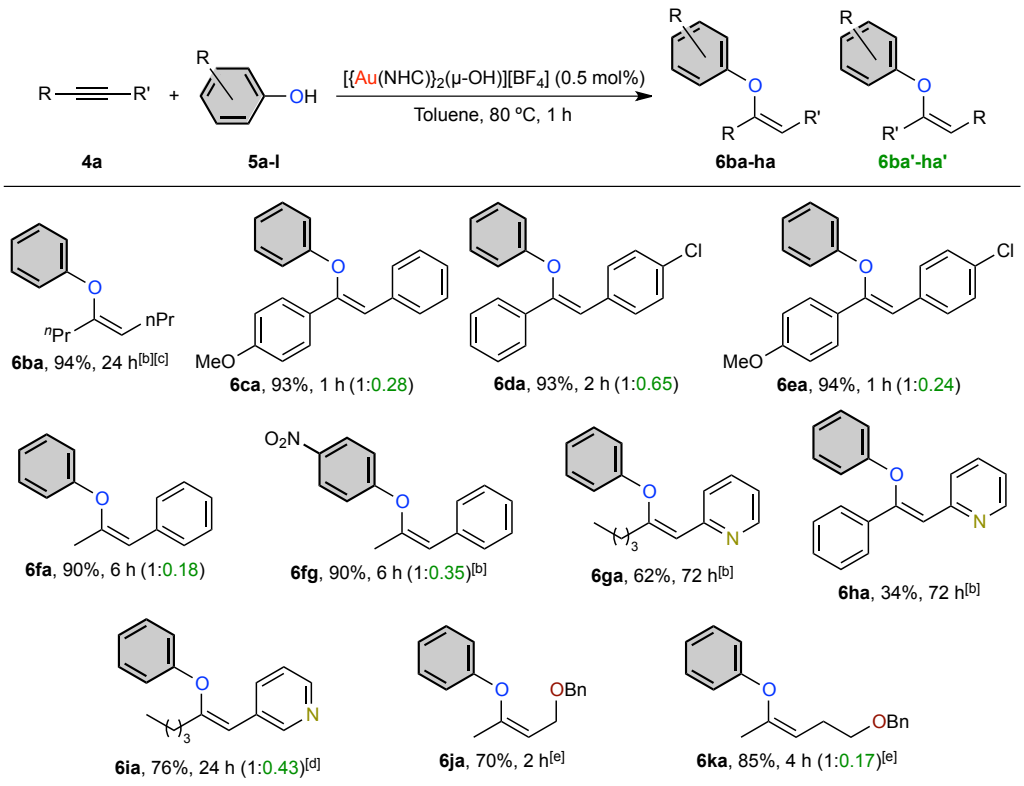


[a] Conditions: **4a** (0.50 mmol), **5a-l** (0.55 mmol, 1.1 equiv.), **1A** (0.5 mol%), toluene (1 mL), 80 °C. Isolated yields. Average of two runs. [b] **1A** (1 mol%), 110 °C.

The reactions between various alkynes **4** and phenol **5a** (Table 3) were then investigated. *Anti*-addition of **5a** to dialkyl-substituted **4b** afforded the desired product **6ba** in 94% isolated yield in a stereospecific manner. The hydrophenoxylation of unsymmetrical diaryl-substituted alkynes **4c-4e** provided the corresponding products **6ca-6ea** stereospecifically in high yields but moderate regioselectivities. Better regioselectivities were observed when one of the aryl moieties bore a methoxy group at the *para*-position, e.g. 1:0.28 *vs.* 1:0.65 (**6ca** and **6da**, Table 3). Aryl-alkyl-alkynes were examined next. Addition of **5a** to 1-phenylpropyne (**4f**) afforded the regioisomers in a 1:0.18 ratio. The reaction of **4f** with 4-nitrophenol (**5g**) instead of **5a** was also investigated. Vinyl ether **6fg** was obtained as the major product. Interestingly, the regioselectivity in this reaction is the opposite of Sahoo's (**6fg** /**6fg'** = 1/0.35 *vs.* 0.61/1), pointing again towards a different reaction mechanism for each methodology.[153] The reactions using alkynes **4g** and **4h**, having a potential directing group such as pyridine, were then tested. Gratifyingly, the reaction proceeded with complete regioselectivity, although at lower rates, affording aryl vinyl ethers **6ga** and **6ha** in moderate and low yields of 62% and 34%

respectively. We hypothesised that this directing effect could be a combination of the charge polarisation on the alkyne and an interaction between the pyridine *N* atom and one of the gold centres. To test our hypothesis we decided to synthesise an alkyne with a similar charge distribution, but bearing a 3-pyridine (**4i**) substituent instead of the 2-pyridine one (**4h**). In order to reduce the reaction time the catalyst loading was increased to 3 mol%. Interestingly, the selectivity dropped dramatically and a 1:0.43 ratio between the two regioisomers was observed (**6ia**, Table 3). Then we decided to reduce the polarisation on the alkyne, but keeping a potential chelating heteroatom to see if we could still observe complete regioselectivity. The hydrophenoxylation of the unsymmetrical propargylic ether **4j** afforded, with complete regioselectivity, the corresponding vinyl ether in good yields (**6ja**, Table 3). As expected, when homopropargylic ether **6k** was used diminished selectivity was observed, 1:0.17 (**6ka**, Table 3). Thus supporting our hypothesis that regioselectivity can be obtained by assistance of a directing group, either by polarisation of the alkyne or by a chelating effect.

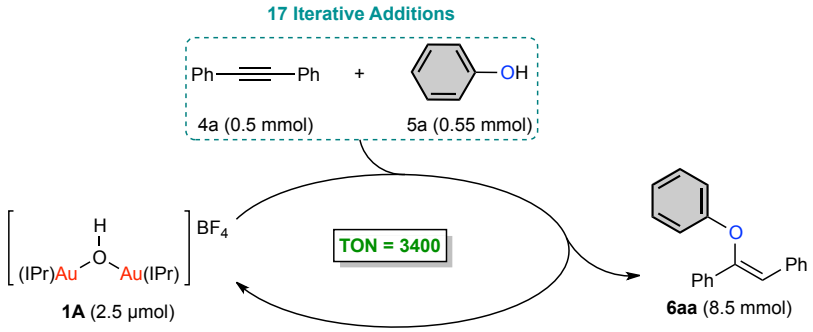
Table 3. Hydrophenoxylation using various unsymmetrical alkynes.[a]



[a] Conditions: **4b-h** (0.50 mmol), **5a** or **5g** (0.55 mmol, 1.1 equiv.), **1A** (0.5 mol%), toluene (1 mL), 80 °C. Isolated yield. Average of two runs. Ratio determined by ^{1}H NMR. [b] **1A** (1 mol%), 110 ºC. [c] **4b** (0.55 mmol) and **5a** (0.50 mmol). [d] **1A** (3 mol%), 110 ºC. [e] Alkyne (2 equiv.).

7.2.3 *Catalyst Recycling*

^{1}H NMR spectra of the crude products revealed that **1A** was still present after the reactions were complete. This prompted us to believe that it may be possible to recycle **1A** once the reaction was complete. Therefore, to assess the recyclability of **1A**, once the reaction between alkyne **4a** and phenol **5a** was complete, iterative additions of both substrates (0.5 and 0.55 mmol, respectively) were conducted. As a result of 17 iterative additions, 8.5 mmol of **4a** were converted over 36 h using 2.5 µmol of **1A** affording an impressive turn over number (TON) of 3400. To relate this to the previous state-of-the-art, Sahoo's procedure afforded a TON of 7 for **6aa** (Scheme 2).[153]



Scheme 2. Iterative additions of **4a** and **5a** to the catalytic reaction.

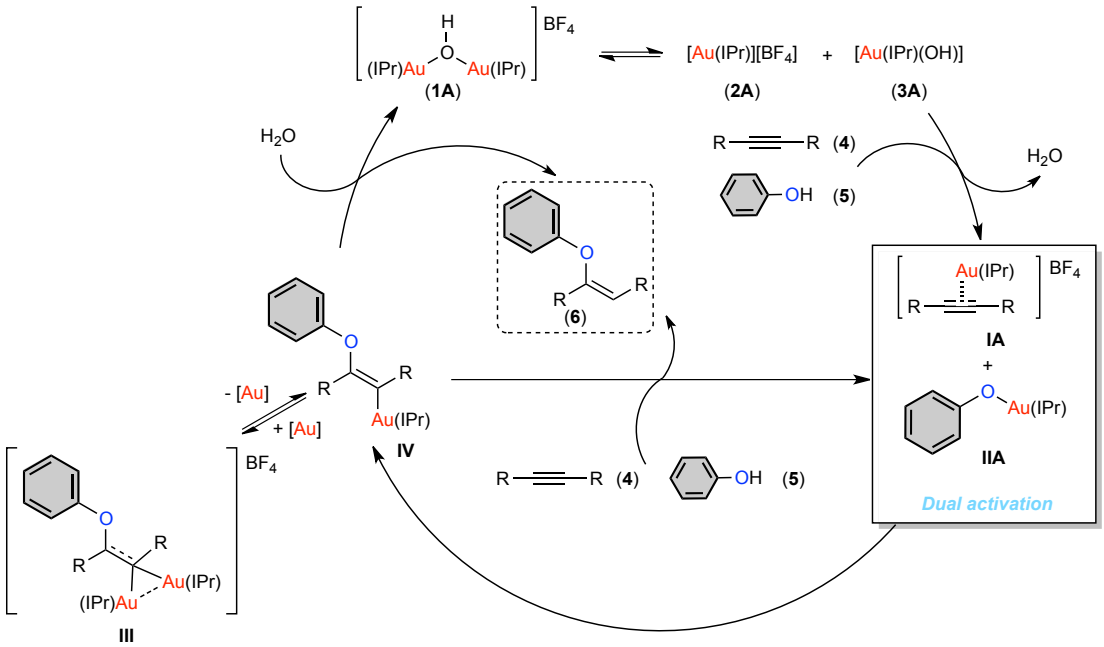
7.2.4 *Competition Experiments: Hydration vs. Hydrophenoxylation*

Since digold-hydroxide **1A** has also proven to be a very active catalyst for alkyne hydration (see Chapter 5),[156] we were surprised to observe no formation of ketone side-products under our standard conditions; *i.e.* using technical grade toluene, under air, and water also being generated during the reaction. Intrigued by this, we decided to study the effect of water on the hydrophenoxylation reaction. Known amounts of water (0.5, 1, 2, 5 and 8 equiv. with respect to phenol) were added to the reaction mixture and the conversion to the final product followed by GC. While the reaction rate decreased, no formation of the expected ketone, or any other side product, could be observed, thus suggesting that the hydrophenoxylation is favoured *versus* hydroxylation under our reaction conditions.

7.2.5 *Mechanistic Studies*

Once the scope and limitations of the system were established, the reaction mechanism was probed. A dual activation mechanism was hypothesised for the hydrophenoxylation of internal alkynes and is depicted in Scheme 3. In this mechanistic scenario, [{Au(IPr)}$_2$(µ-OH)][BF_4] (**1A**) is in equilibrium with [Au(IPr)][BF_4] (**2A**) and [Au(IPr)(OH)] (**3A**) under the reaction conditions. [Au(IPr)][BF_4] (**2A**) activates alkyne **4** to form the π-gold-alkyne

complex **IA**,[154] while [Au(IPr)(OH)] (**3A**) reacts with phenol **5** to provide the gold phenoxide complex **IIA**.[44-45] The latter then attacks from the opposite side of **IA** to give a *gem*-diaurated compound **III**[52,60,61b,64c-e,64g,65] or σ-monoaurated compound **IV**[64b,140a,157] along with [Au(IPr)][BF_4] (**2A**). Similar intermediates have recently been proposed for the addition of MeOH to alkynes.[140b,158] Finally, protodeauration of **IV** with phenol **5** or H_2O takes place to afford vinyl ether **6** (Scheme 3).



Scheme 3. Proposed reaction mechanism.

7.2.5.1 Catalyst Dissociation

To support our proposed mechanism, the possible equilibrium between **1A**, **2A** and **3A** was examined. When mixing [{Au(IPr)}$_2$(μ-OH)][BF_4] (**1A**) and [{Au(SIPr)}$_2$(μ-OH)][BF_4] (**1B**)[123] a statistical distribution (1:1:2) was observed by ^{1}H NMR spectroscopy between the peaks corresponding to the OH of **1A**, **1B** and the cross-over product [{Au(IPr)}{Au(SIPr)}(μ-OH)][BF_4] (**1C**) (Figure 1). This result strongly supports the existence of the aforementioned equilibrium.

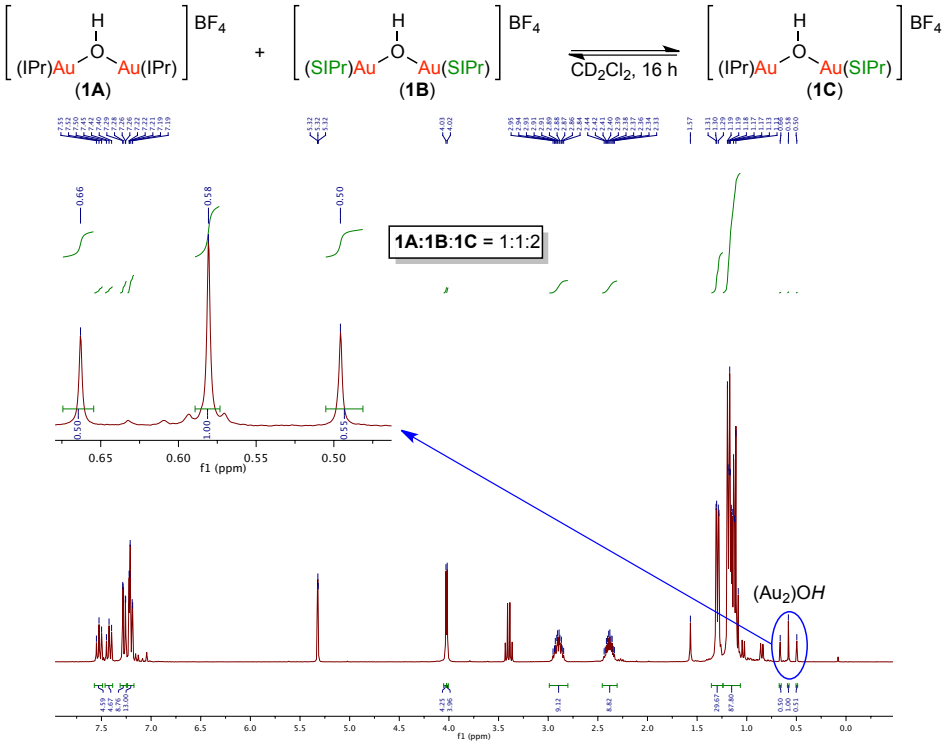
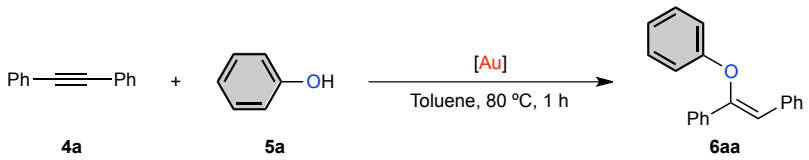


Figure 1. Equilibrium between **1A**, **1B** and the crossover product **1C**

7.2.5.2 Catalytically Active Species

Next, the use of **2A** and **3A** as catalysts was investigated (Table 4). Since **2A** is not a stable species, three different sources of $[Au]^+$ were examined: $[Au(IPr)(CH_3CN)][BF_4]$ (**2A'**), [Au(IPr)(OTf)] (**2A''**) and $[Au(IPr)(NTf_2)]$ (**2A'''**).[22a] The use of 1 mol% of the cationic species **2A'** afforded 40% conversion to the desired vinyl ether **6aa**, after 1 h, while neutral complexes **2A''** and **2A'''** showed very poor reactivity, 14% and 1%, respectively (Entries 1-3, Table 4). We have previously postulated that **2A'** could lead to *in situ* generation of **1A** in the presence of water, while the neutral species **2A''** and **2A'''** cannot (See Chapter 5 for more details).[31a] Since the reaction was carried out using technical grade toluene and under air, this could explain the higher conversions observed using **2A'** as catalyst. To confirm this, the reaction using **2A'** was repeated in the presence of 3 drops of water. An improved conversion of 81% was observed, whereas under anhydrous conditions poorer conversions were obtained (Entries 4-5, Table 4). Next, we examined the ability of [Au(IPr)(OH)] **3A** to catalyse the hydrophenoxylation of alkynes. As expected, **3A** performed vey poorly and gave only 1% conversion (Entry 6, Table 4). This, along with the previous series of experiments unequivocally establishes that **2A** can catalyse the hydrophenoxylation of alkynes, although not as efficiently as digold hydroxide **1A**; and that **3A** alone cannot catalyse the reaction. Nevertheless, the combination of both **2A'** (0.5 mol%) and **3A** (0.5 mol%) showed high conversion (87%) (Entry 7, Table 4).

Table 4. Catalytic studies[a]



4a **5a** **6aa**

Entry	Catalyst (mol%)	Conversion (%)[b]
1	(**2A'**) [Au(IPr)(CH_3CN)][BF_4] (1)	40
2	(**2A''**) [Au(IPr)(OTf)]	15
3	(**2A'''**) [Au(IPr)(NTf_2]	1
4	**2A'** (1) + H_2O	81
5[c]	**2A'** (1)	33
6	(**3A**) [Au(IPr)(OH)]	< 1
7	**2A'** (0.5) + **3A** (0.5)	87

[a] Conditions: **4a** (0.50 mmol), **5a** (0.55 mmol, 1.1 equiv.), toluene (1 mL), 80 °C. [b] Conversions determined by GC. Average of two runs. [c] Anhydrous conditions.

Intrigued by the differences observed between **2A'**, **2A''** and **2A'''** we wondered whether the reaction could be influence by the counterion in **1A**. Therefore, we decided to synthesise a series of digold-hydroxide species [{Au(IPr)}$_2$(μ-OH)][X], where X = BF_4 (**1A**), FABA (tetrakis(pentafluorophenyl)borate, **1Aa**), SbF_6 (**1Ab**), OTf (**1Ac**) or NTf_2 (**1Ad**),[31a] and study how the counterion affected their catalytic activity (Figure 1). As expected, complexes **1A**-**1Ab**, bearing classical non-coordinating outer-sphere counter-ions, afforded very good conversions after 1 h at 80 ºC; while **1Ad**, bearing a highly coordinating inner-sphere counter-ion, showed very poor activity. Interestingly, complex **1Ac**, bearing a less coordinating counter-ion, afforded moderate conversions to the desired product (Figure 2).

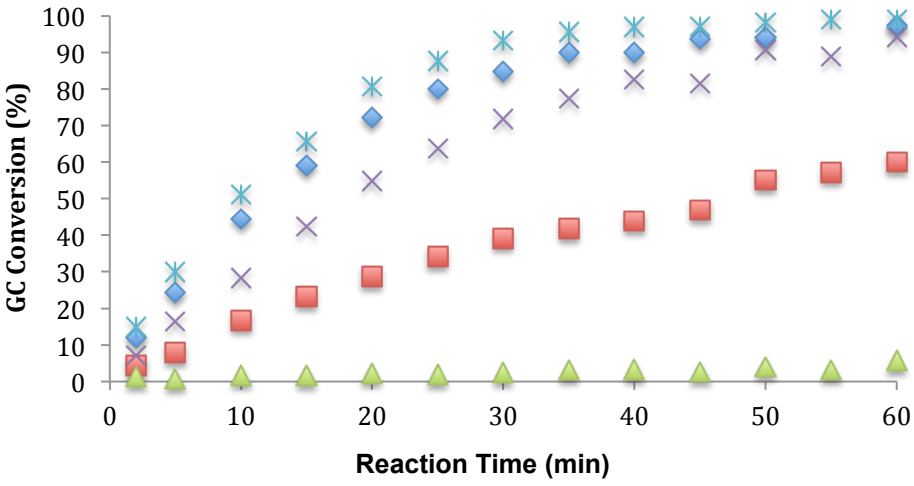
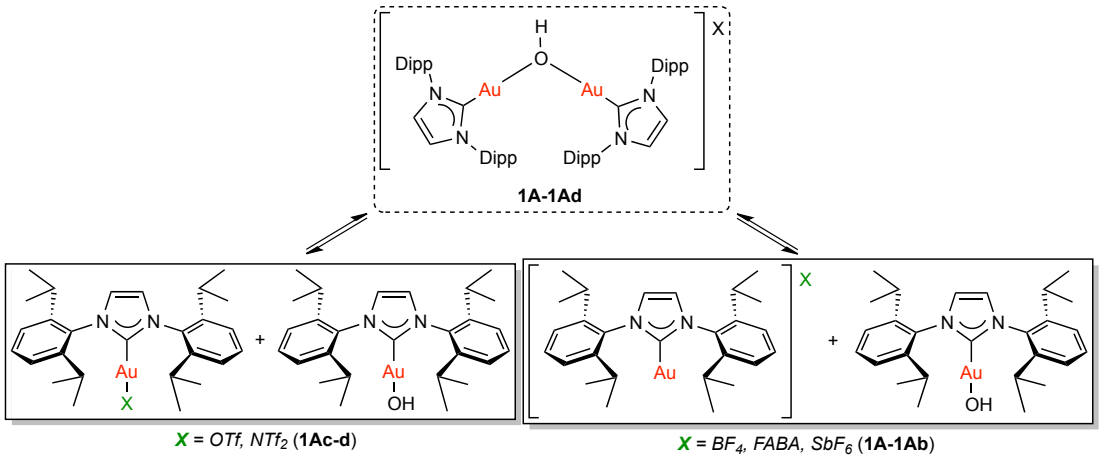


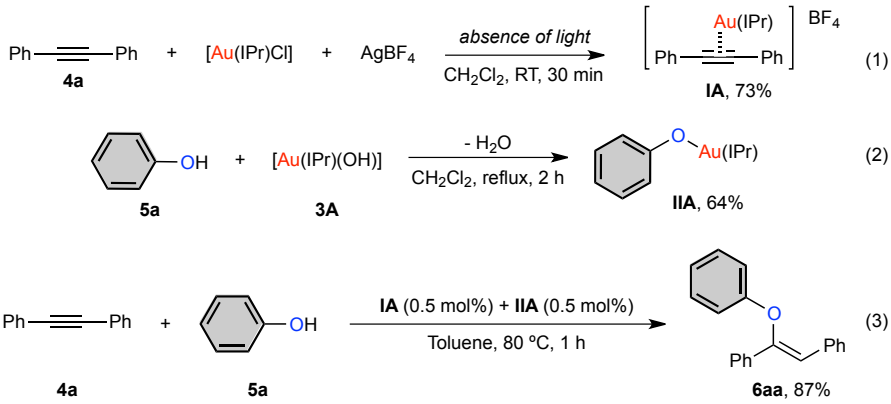
Figure 2. Counterion effect on the hydrophenoxylation of alkynes.[a] Reaction conditions: Diphenylacetylene (0.50 mmol, 1 equiv.), phenol (0.55 mmol, 1.1 equiv.), [Au] (2.5 μmol, 0.5 mol%), toluene (1 mL), 80 ºC. [Au_2OH][NTf_2] (▲), [Au_2OH][OTf] (■), [Au_2OH][SbF_6] (×), [Au_2OH][BF_4] (◆), [Au_2OH][FABA] (✳). Average of at least 2 runs.

We hypothesised that these differences in reactivity may therefore be related to the dissociation of complex **1**. While complexes **1A-Ab** would dissociate into gold-hydroxide [Au(IPr)OH] **3A**, and cationic species [Au(IPr)][X] (**2A-Ab**); complexes **1Ac-d** would dissociate into **3A** and neutral species [Au(IPr)(X)] (**2Ac-d**) (Scheme 4). Activation of the alkyne might be easier by cationic species **2A-Ab** than by the neutral ones (**2c-d**). This is also reflected in the reactivity pattern of the mononuclear species, where cationic [Au(IPr)(MeCN)][BF_4] (**2A'**) afforded higher conversions (40%) than neutral species [Au(IPr)(OTf)] (**2A''**) (14%), bearing a labile inner-sphere counter-ion, or [Au(IPr)(NTf_2)] (**2A'''**) (1%), bearing a more tightly coordinated inner-sphere counter-ion.



Scheme 4. Dissociation of **1A-Ad** into cationic/neutral species and gold hydroxide depending on the counterion

Next, π-gold-alkyne complex **IA**[154] and gold-phenoxide complex **IIA**[44-45] were synthesised following the reported methodologies and tested in catalysis: a) π-gold-alkyne complex **IA** was synthesised in good yield (eq. 1, Scheme 5), by adding $AgBF_4$ to a mixture of [Au(IPr)Cl] and diphenylacetylene (**4a**) and b) gold-phenoxide **IIA** was synthesised by mixing [Au(IPr)(OH)] (**3A**) and phenol (**5a**) (eq. 2, Scheme 5). Gratifyingly, the combination of both **IA** (0.5 mol%) and **IIA** (0.5 mol%) afforded 87% conversion to the desired product **6aa** (eq. 3, Scheme 5). These results are consistent with our proposal that a digold hydroxide species **1** can act as cooperative bifunctional catalysts to permit the efficient hydrophenoxylation of alkynes.

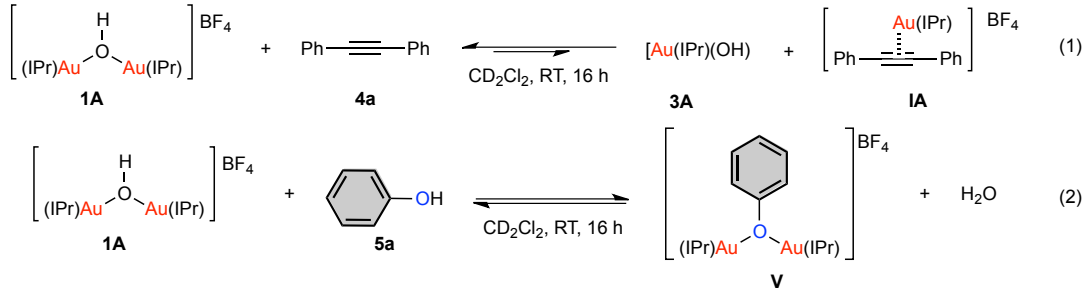


Scheme 5. Testing **IA** and **IIA** as catalytic species

7.2.5.3 Stoichiometric Studies

To further support our hypothesis of dual gold activation, a number of stoichiometric reactions were carried out. Due to solubility problems in toluene-d^8, experiments were carried out in CD_2Cl_2. Also, as the presence of water can displace equilibria towards formation of **1A**, anhydrous conditions were used.

First we investigated if **1A** could interact with either of the substrates. After 16 h at room temperature no reaction was observed between **1A** and alkyne **4a**. However, complete conversion into **1A** and **4a** was observed when mixing **3A** and π-complex **I**, strongly suggesting the existence of an equilibrium between these species which is strongly in favour of **1A** and **4a** (eq. 1, Scheme 6). When reacting **1A** and phenol **5a**, *ca.* 50% conversion to a new species could be observed. In the presence of molecular sieves, only one species was observed. ^{1}H and ^{13}C{^{1}H} NMR spectroscopy as well as elemental analysis confirmed that this new species as [{Au(IPr)}$_2$(μ-OPh)][BF$_4$] (**V**) (eq. 2, Scheme 6). Crystals suitable for X-ray diffraction analysis were grown by slow diffusion of pentane over a saturated solution of **V** in CH_2Cl_2 at –35 ºC (Figure 3)



Scheme 6. Interaction of **1A** with **4a** and **5a**

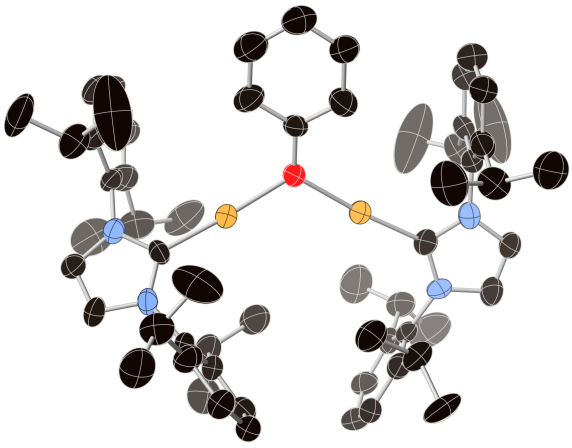
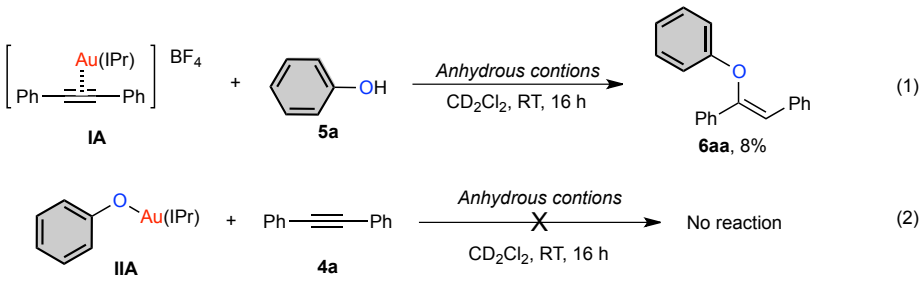


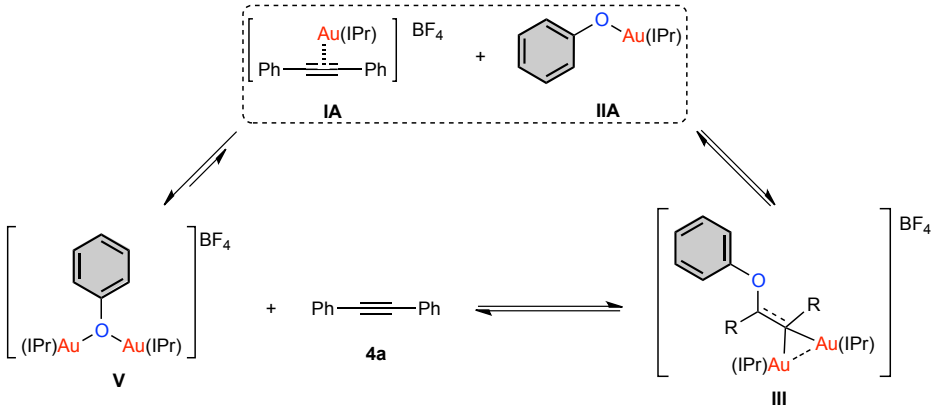
Figure 3. Thermal ellipsoid representation of diaurated species **V**. Counterion omitted for clarity.

The interactions between **IA**, **IIA**, **4a** and **5a** were also examined. Only 8% conversion to **6aa** was observed when reacting phenol **5a** and **IA** for 16 h at room temperature (eq. 1, Scheme 7). Moreover, no reaction was observed between alkyne **4a** and phenoxide **IIA** under identical reaction conditions (eq. 2, Scheme 7).



Scheme 7. Interaction between the proposed intermediates, **IA** and **IIA**, and substrates **4a** and **5a**.

Next, the interaction between the proposed reaction intermediates was examined. We were pleased to observe that the reaction between π-complex **IA** and **IIA** occurred within mixing time (Scheme 8). After 5 min, complete consumption of the starting materials was observed and two new species were detected by ^{1}H NMR spectroscopy in a 1:3 ratio. The minor species was identified as digold phenoxide **V**. We hypothesised that **V** may be in equilibrium with **IA**, **IIA** and alkyne **4a**. This equilibrium favours formation of the diaurated species **V**, the same as the equilibrium in eq. 1, Scheme 6 favouring formation of **1A**. In addition, we postulated that the major species could be the *gem*-diaurated complex **III** and what is observed is an equilibrium between **V**, **4a** and **III** (Scheme 8).



Scheme 8. Equilibria between **IA**, **IIA**, **V**, **4a** and **III.**

In order to test this hypothesis, an excess of alkyne **4a** was added to the reaction mixture to attempt to displace the equilibrium towards formation of **III**. Gratifyingly, the latter and **4a** are observed. Unfortunately, attempts to isolate the *gem*-diaurated species **III** were not successful as once the excess of **4a** is removed a mixture between digold-phenoxide **V**, **4a** and **III** was obtained, further supporting the hypothesis that this step is an equilibrium (Figure 4).

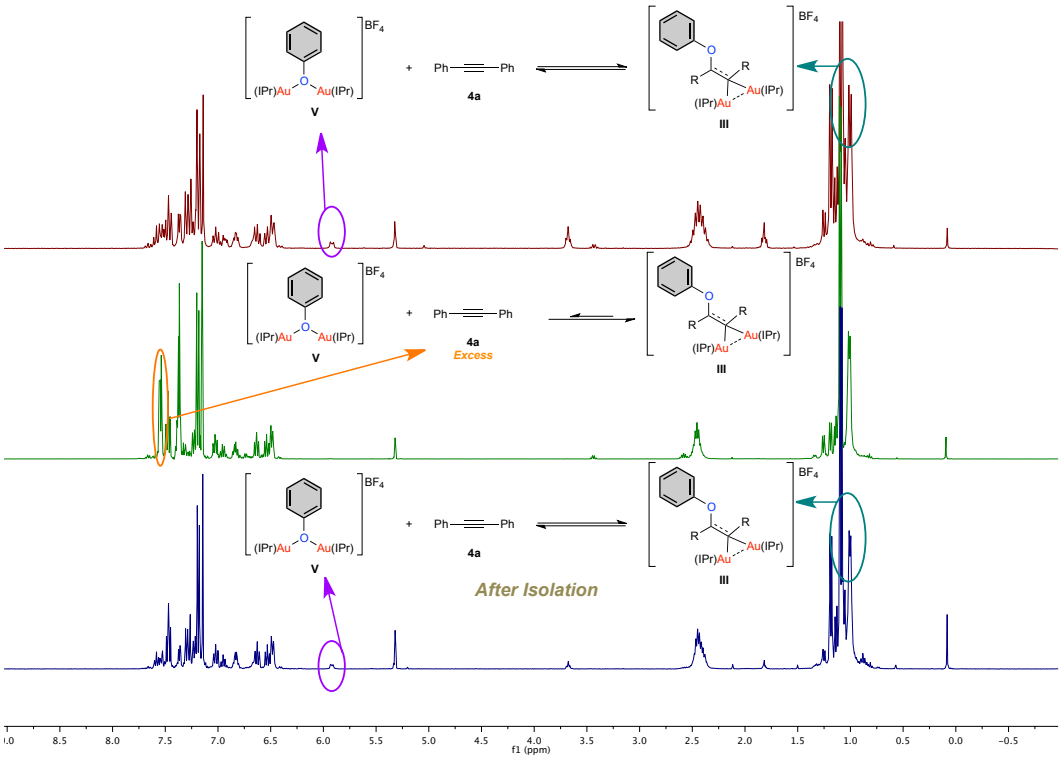
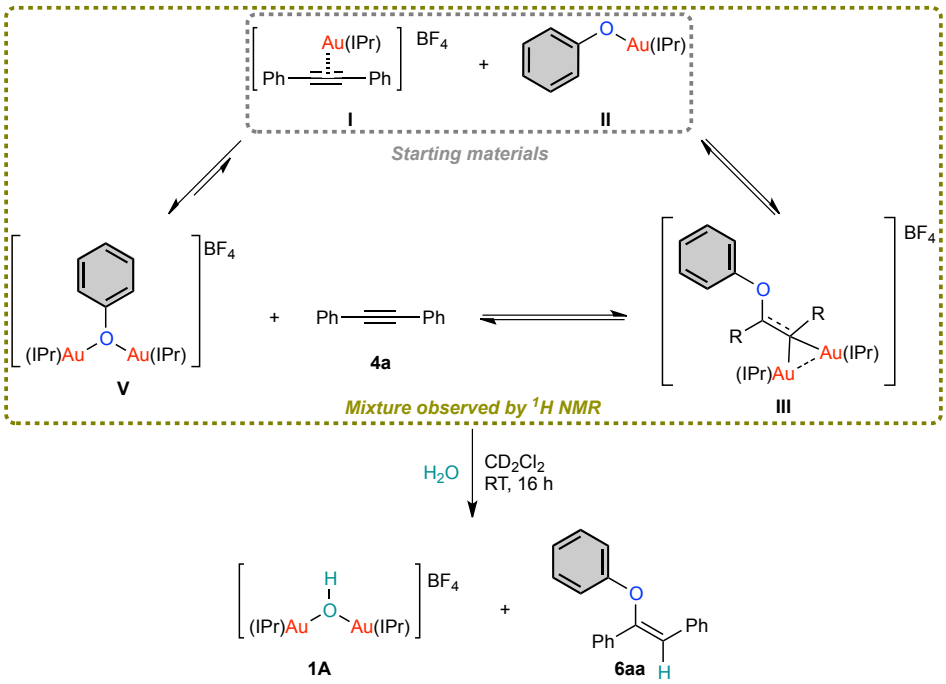


Figure 3. Study of the equilibrium between **V**, **4a** and **III**.

If the reaction mixture of π-complex **I** and gold-phenoxide **II** is quenched with H_2O, complete conversion to the desired vinyl ether **6aa** and digold hydroxide **1A** can be observed

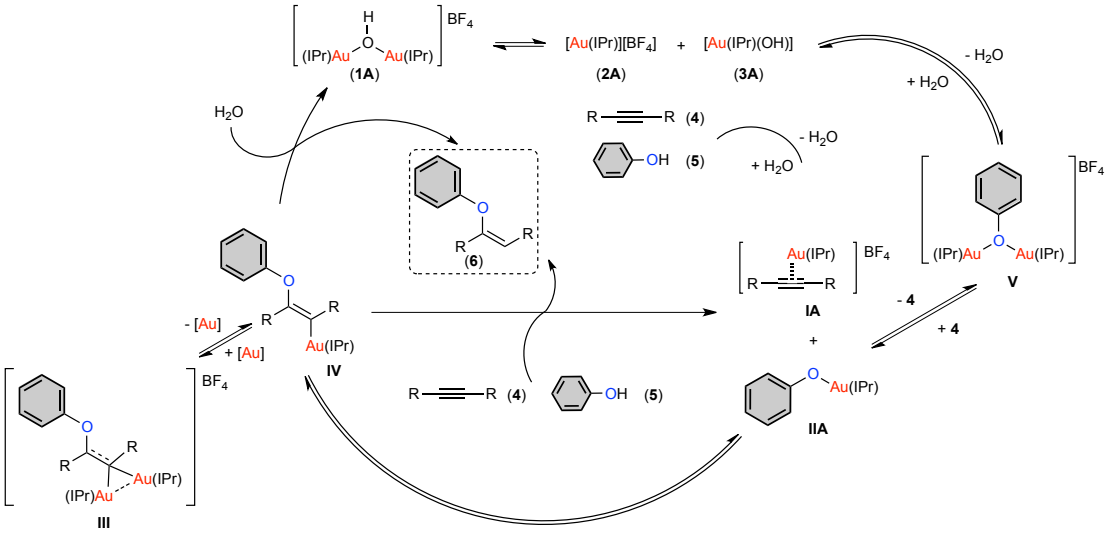
(Scheme 9). This suggests that the protodeauration step can take place either *via* water present in the reaction or *via* the more acidic proton of the phenol.



Scheme 9. Protodeauration *via* water

Taking all the new information into account, an updated catalytic cycle can be proposed (Scheme 10). The main addition, in comparison to the previously postulated mechanism, is the inclusion of digold-phenoxide **V** and the series of equilibria where it is involved. Thus, the first step might be the reaction between **1A** and phenol (**5**), resulting in the formation of diaurated species **V**. Then, upon interaction of the latter with alkyne (**4**), gem-diaurated species **III** is formed. The existence of an equilibrium between **V**, **4a** and **III** that suggests the possibility of a reversible C-O bond formation. A similar reversible C-O bond formation has been reported by Gagné and Widenhoefer for the intramolecular hydroxalkoxylation of allenes.[65] Next, the protodeauration step would take place *via* vinyl-gold intermediate **IV** rather than *via* *gem*-diaurated complex **III**, thus **III** would be an off-cycle species. This assumption is based on the reactivity studies performed by Gagné and co-workers on *gem*-diaurated species (see Chapter 1 for more information), in which they proposed that the protodeauration of vinyl-gold complexes is more facile than that of their *gem*-diaurated counterparts.[61a] The same behaviour was later observed by Gagné and Widenhoefer for the intramolecular hydroxalkoxylation of allenes.[65] Finally, the experiments that we have performed suggest that the protodeauration step is the only irreversible step within the proposed catalytic cycle, and that it can proceed *via* water or phenol. In addition, while there are several examples describing the interaction of *two* gold centres with *one* substrate

molecule,[53] generally intramolecular reactions, to the best of our knowledge this dual gold-catalysed hydrophenoxylation of alkynes represent the first example of the interaction of *two* gold centres with *two* substrate molecules.



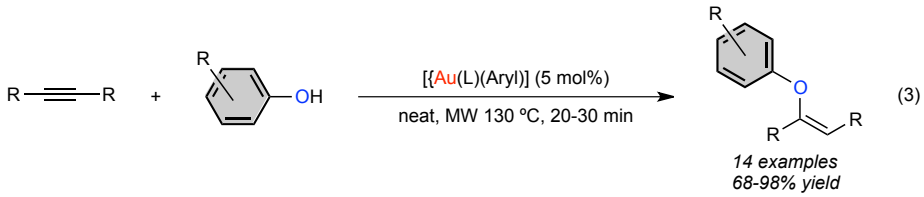
Scheme 10. Updated catalytic cycle

7.3 Conclusion

In summary, we have developed a mild and straightforward methodology for the hydrophenoxylation of alkynes, using digold-hydroxide complexes, to form various aryl vinyl ethers in good to high yields with good regioselectivities. Moreover, preliminary studies on directing group effects suggest that it could be possible to achieve complete regiocontrol on the addition of phenols to unsymmetrically substituted alkynes. In addition, the current data strongly support a dual activation pathway; where digold hydroxide **1A** dissociates into a Lewis acid **2A** and a Brønsted base **3A** whereupon these species will independently react with substrates **4** and **5** respectively. Alternatively, **1A** can react with phenol (**5**), thus forming digold-phenoxide **V**. This species can then react with alkyne (**4**) forming **IA** and **IIA**, which would lead to the formation of *gem*-diaurated species **III**. At the moment, all evidence points towards this intermediate being an off-cycle species and that the protodeauration step takes place *via* vinyl-gold intermediate **IV**. To the best of our knowledge this reaction represents the first example of *two* gold centres interacting with *two* substrate molecules. Due to this synergistic effect, the hydrophenoxylation of alkynes proceeds smoothly under relatively mild conditions. These findings provide new insights into the chemistry of gold catalysis and open the door to the development of new catalytic transformations based on dual activation.

After our findings were published, Stockland and co-workers reported the third study on gold-catalysed hydrophenoxylation of alkynes.[159] They synthesised several [Au(L)(aryl)] (L =

PR_3 or NHC) complexes and tested their activity in the hydrophenoxylation reaction without the need for an external base and using microwave irradiation (eq. 3).



(3)

7.4 Experimental Section

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. Deuterated solvents (CD_2Cl_2, $CDCl_3$) were filtered through basic alumina in order to remove traces of HCl. NMR spectra were recorded on 400 and 300 MHz spectrometers at room temperature in CD_2Cl_2 or $CDCl_3$. Chemical shifts (δ) are reported in ppm, relative to the solvent residual peak CD_2Cl_2 (5.32 ppm for ^1H and 54.00 ppm for ^{13}C) and $CDCl_3$ (7.26 ppm for ^1H and 77.16 ppm for ^{13}C). Data for ^1H NMR spectra are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, br = broad signal, m = multiplet), coupling constants (*J*) in Hz and integration. For the assignment of the ^1H and $^{13}C\{^1H\}$ NMR spectra of gold complexes **IA**, **IIA**, **III** and **V** [^1H, ^1H] COSY, [^1H, ^{13}C] HSQC and [^1H, ^{13}C] HMBC experiments were also performed. Flash chromatography was performed on silica gel 60 Å pore diameter and 40-63 μm particle size. Elemental analyses were carried out by the analytical services of London Metropolitan University. High-resolution mass spectrometry was performed by the EPSRC National Mass Spectrometry Service Centre (NMSSC) (Grove Building Extn., Swansea University, Singleton Park, Swansea, SA2 8PP, U.K.). $[\{Au(NHC)\}_2(\mu\text{-OH})][BF_4]$ (NHC = IPr, SIPr, IPr^{Cl} and IPent) were synthesised according to our previous report (See Chapters 4 and 5).[31b,123] $[\{Au(IPr)\}_2(\mu\text{-OH})][X]$ complexes **1A-1Ad** were synthesise according to literature procedures.[31a]

General procedure for the hydrophenoxylation of alkynes: $[\{Au(NHC)\}_2(\mu\text{-OH})][BF_4]$ (0.5 or 1.0 mol%) was added to a solution of alkyne (0.5 mmol) and phenol (0.55 mmol, 1.1 equiv) in toluene (1 mL). The reaction mixture was stirred at 80 or 110 °C. After the reaction was completed, the solvent was concentrated in vacuum. The residue was purified by flash column chromatography on silica gel to give the corresponding product.

*(Z)-(1-Phenoxyethene-1,2-diyl)dibenzene (**6aa**):*According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), phenol (**5a**) (52.0 mg, 0.55 mmol) and $[\{Au(IPr)\}_2(\mu\text{-OH})][BF_4]$ (3.2 mg, 0.25 mmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 1 h, was purified by column chromatography on silica

gel (*n*-hexane/EtOAc = 95/5) to give **6aa** (130 mg, 96%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.68-7.62 (m, 2H), 7.62-7.56 (m, 2H), 7.3-7.16 (m, 8H), 7.06-6.98 (m, 2H), 6.98-6.90 (m, 1H), 6.66 (s, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 156.4, 149.7, 136.1, 134.8, 129.8, 129.1, 128.69, 128.65, 128.5, 127.5, 126.2, 122.1, 116.9, 116.4.

*(Z)-[1-(4-Methoxyphenoxy)ethene-1,2-diyl]dibenzene (**6ab**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 4-methoxyphenol (**5b**) (68.3 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ab** (149 mg, 98%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.69-7.61 (m, 2H), 7.61-7.53 (m, 2H), 7.40-7.14 (m, 6H), 7.01-6.88 (m, 2H), 6.81-6.67 (m, 2H), 6.60 (s, 1H), 3.71 (s, 3H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 154.7, 150.31, 150.26, 136.2, 135.09, 129.0, 128.7, 128.5, 127.4, 126.4, 117.3, 116.7, 114.9, 55.7.

*(Z)-[1-(4-Methylphenoxy)ethene-1,2-diyl]dibenzene (**6ac**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), *p*-cresol (**5c**) (59.4 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ac** (140 mg, 97%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.68-7.61 (m, 2H), 7.61-7.54 (m, 2H), 7.37-7.17 (m, 6H), 7.05-6.97 (m, 2H), 6.95-6.85 (m, 2H), 6.63 (s, 1H), 2.23 (s, 3H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 154.3, 150.0, 136.2, 135.0, 131.4, 130.2, 129.0, 128.62, 128.61, 128.4, 127.4, 126.2, 116.7, 116.2, 20.6.

*(Z)-[1-(4-Fluorophenoxy)ethene-1,2-diyl]dibenzene (**6ad**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 4-fluorophenol (**5d**) (61.7 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ad** (142 mg, 98%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.68-7.60 (m, 2H), 7.60-7.52 (m, 2H), 7.39-7.18 (m, 6H), 7.02-6.84 (m, 4H), 6.64 (s, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 158.0 (d, $J_{C\text{-}F}$ =

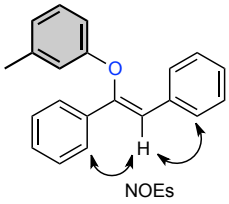
240 Hz), 152.3, 149.9, 135.8, 134.7, 129.0, 128.72, 128.67, 128.6, 127.6, 126.2, 117.4 (d, JC-F = 8.1 Hz), 116.9, 116.3 (d, $J_{C\text{-}F}$ = 24 Hz). **^{19}F{^{1}H} NMR** ($CDCl_3$, 282 MHz) δ -122.5.

*(Z)-[1-(4-Chlorophenoxy)ethene-1,2-diyl]dibenzene (**6ae**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 4-chlorophenol (**5e**) (70.7 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ae** (144 mg, 94%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.67-7.49 (m, 4H), 7.38-7.12 (m, 8H), 7.00-6.90 (m, 2H), 6.67 (s, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 155.0, 149.5, 135.6, 134.6, 129.8, 129.1, 128.8, 128.7, 127.7, 127.1, 126.1, 117.7, 117.1.

*(Z)-{[1-(4-Trifluoromethyl)phenoxy]ethene-1,2-diyl}dibenzene (**6af**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 4-(trifluoromethyl)phenol (**5f**) (89.2 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 4 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6af** (155 mg, 91%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.65-7.54 (m, 4H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.41-7.17 (m, 6H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.73 (s, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 159.1, 149.0, 135.4, 134.4, 129.1, 128.91, 128.86, 128.8, 127.9, 127.3 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125.9, 124.4 (q, $J_{C\text{-}F}$ = 271 Hz), 124.3 (q, $J_{C\text{-}F}$ = 33 Hz), 117.3, 116.4. **^{19}F{^{1}H} NMR** ($CDCl_3$, 282 MHz) δ -62.2.

*(Z)-[1-(4-Nitorophenoxy)ethene-1,2-diyl]dibenzene (**6ag**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 4-nitrophenol (**5g**) (77.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 9/1) to give **6ag** (154 mg, 97%, average of two runs) as a pale yellow liquid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.20-8.08 (m, 2H), 7.62-7.50 (m, 4H), 7.44-7.18 (m, 6H), 7.17-7.05 (m, 2H), 6.78 (s, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 161.6, 148.6, 142.7, 134.9, 133.9, 129.1, 129.0, 128.8, 128.1, 126.2, 125.7, 117.4, 116.4.

*(Z)-[1-(3-Methylphenoxy)ethene-1,2-diyl]dibenzene (**6ah**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), *m*-cresol (**5h**) (59.4 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ah** (139 mg, 97%, average of two runs) as a white solid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.74-7.50 (m, 4H), 7.40-7.16 (m, 6H), 7.09 (*J* = 8.0 Hz, 1H), 6.87 (brs, 1H), 6.84-6.72 (m, 2H), 6.65 (s, 1H), 2.27 (s, 3H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 156.4, 149.8, 139.9, 136.2, 134.9, 129.4, 129.1, 128.7, 128.4, 127.5, 126.1, 123.0, 117.1, 116.8, 113.4, 21.6. **HRMS** (APCI) calcd for $C_{21}H_{19}O$ [$(M+H)^+$] 287.1430, found 287.1428.

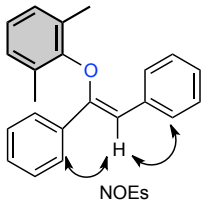


*(Z)-[1-(3-Fluorophenoxy)ethene-1,2-diyl]dibenzene (**6ai**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 3-fluorophenol (**5i**) (61.7 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ai** (138 mg, 94%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.67-7.51 (m, 4H), 7.40-7.07 (m, 7H), 6.85-6.79 (m, 1H), 6.78-6.71 (m, 1H), 6.69 (s, 1H), 6.69-6.61 (m, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 163.7 ($J_{C\text{-}F}$ = 245 Hz), 157.7 ($J_{C\text{-}F}$ = 10 Hz), 149.3, 135.6, 134.5, 130.6 ($J_{C\text{-}F}$ = 9.8 Hz), 129.1, 128.8, 128.69, 128.68, 127.7, 126.0, 117.1, 112.1 ($J_{C\text{-}F}$ = 2.9 Hz), 109.1 ($J_{C\text{-}F}$ = 22 Hz), 104.2 ($J_{C\text{-}F}$ = 25 Hz). **^{19}F{^{1}H} NMR** ($CDCl_3$, 282 MHz) δ -111.7.

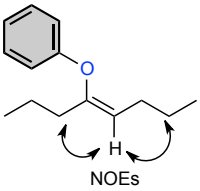
*(Z)-[1-(2-Methylphenoxy)ethene-1,2-diyl]dibenzene (**6aj**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), *o*-cresol (**5j**) (59.4 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6aj** (142 mg, 99%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.66-7.59 (m, 2H), 7.58-7.49 (m, 2H), 7.36-7.15 (m, 7H), 6.98-6.79 (m, 2H), 6.71 (d, *J* = 7.8 Hz, 1H) 6.66 (s, 1H), 2.52 (s, 3H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 154.3, 150.0, 136.2, 135.0, 131.2, 128.9, 128.7, 128.6, 128.5, 127.4, 127.0, 126.7, 125.9, 121.9, 116.7, 114.4, 16.6.

*(Z)-[2-(1,2-Diphenylvinyloxy)]biphenyl (**6ak**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 2-phenylpenol (**5k**) (93.6 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ak** (154 mg, 89%, average of two runs) as a white solid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.76-7.68 (m, 2H), 7.66-7.57 (m, 2H), 7.54-7.33 (m, 6H), 7.34-7.15 (m, 6H), 7.14-6.96 (m, 2H), 6.90 (dd, *J* = 8.0, 1.4 Hz, 1H) 6.62 (s, 1H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 153.1, 150.2, 138.3, 136.0, 134.9, 131.5, 131.2, 129.8, 129.0, 128.7, 128.6, 128.6, 128.5, 128.3, 127.4, 127.3, 126.1, 122.4, 116.7, 115.6.

*(Z)-[1-(2,6-Dimethylphenoxy)ethene-1,2-diyl]dibenzene (**6al**):* According to the general procedure, a crude product, which was prepared from diphenylacetylene (**4a**) (89.0 mg, 0.50 mmol), 2,6-dimethylphenol (**5l**) (67.2 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 19 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **4al** (101 mg, 67%, average of two runs) as a white solid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.81 (d, *J* = 7.2 Hz, 2H), 7.43-7.29 (m, 4H), 7.27-7.16 (m, 4H), 6.94-6.78 (m, 3H), 6.01 (s, 1H) 2.32 (s, 6H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 154.5, 152.7, 136.6, 136.3, 129.3, 129.2, 129.0, 128.9, 128.4, 128.1, 127.2, 126.6, 123.7, 111.5, 17.4. **HRMS** (APCI) calcd for $C_{22}H_{21}O$ [$(M+H)^+$] 301.1587, found 301.1585.



*(Z)-(4-Octen-4-yloxy)benzene (**6ba**):* According to the general procedure, a crude product, which was prepared from 4-octyne (**4b**) (60.6 mg, 0.55 mmol), phenol (**5a**) (47 mg, 0.50 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ba** (96 mg, 94%, average of two runs) as a colorless liquid. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.37-7.24 (m, 2H), 7.03-6.90 (m, 3H), 5.05 (t, *J* = 7.3 Hz, 1H), 2.12 (t, *J* = 7.3 Hz, 2H), 2.03 (dt, *J* = 7.3, 7.3 Hz, 2H), 1.51 (tq, *J* = 7.3, 7.3 Hz, 2H), 1.39 (tq, *J* = 7.3, 7.3 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** ($CDCl_3$, 101 MHz) δ 156.9, 150.6, 129.6, 121.4, 116.3, 116.1, 34.5, 27.4, 22.9, 20.3, 14.0, 13.7. **HRMS** (APCI) calcd for $C_{14}H_{20}O$ [$(M+H)^+$] 205.1587, found 205.1586.



*(Z)-1-Methoxy-4-(1-phenoxy-2-phenylvinyl)benzene (**6ca**) and (Z)-1-Methoxy-4-(2-phenoxy-2-phenylvinyl)benzene (**6ca'**) (**6ca/6ca'** = 1/0.28):* According to the general procedure, a crude product, which was prepared from **4c**[160] (104.0 mg, 0.50 mmol), phenol

(**5a**) (52.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give the inseparable mixture of **6ca** and **6ca'** (**6ca**/**6ca'** = 1/0.28, 140 mg, 93%, average of two runs) as a white solid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.70-7.45 (m, 4+1.12H), 7.37-7.13 (m, 5+1.40H), 7.08-6.89 (m, 3+0.84H), 6.89-6.77 (m, 2+0.56H), 6.65 (s, 0.28H), 6.56 (s, 1H), 3.79 (s, 3+0.84H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ159.9, 158.9, 156.5, 149.6, 147.9, 136.2, 135.1, 130.4, 129.7, 128.8, 128.63, 128.59, 128.5, 128.1, 127.5, 127.1, 125.8, 122.0, 116.4, 116.2, 115.1, 114.1, 55.32, 55.28.

*(Z)-1-Chloro-4-(2-phenoxy-2-phenylvinyl)benzene (**6da**) and (Z)-1-Chloro-4-(1-phenoxy-2-phenylvinyl)benzene (**6da'**) (**6da**/**6da'** = 1/0.65):* According to the general procedure, a crude product, which was prepared from **4d**[160] (106.3 mg, 0.50 mmol), phenol (**5a**) (52.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give the inseparable mixture of **6da** and **6da'** (**6da** /**6da'** = 1/0.65, 143 mg, 93%, average of two runs) as a white solid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.68-7.42 (m, 4 + 2.60H), 7.47-7.16 (m, 7 + 4.55H), 7.05-6.89 (m, 3 + 1.95H), 6.63 (s, 0.65H), 6.61 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 156.20, 156.16, 150.3, 148.7, 135.8, 134.6, 134.5, 134.3, 133.4, 132.9, 131.7, 130.3, 129.8, 129.1, 128.9, 128.8, 128.7, 128.7, 128.5, 127.7, 127.4, 126.2, 122.4, 122.3, 117.3, 116.3, 115.5.

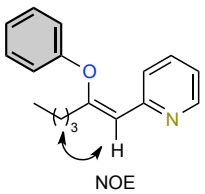
*(Z)-1-Chloro-4-[2-(4-methoxyphenyl)-2-phenoxyvinyl]benzene (**6ea**) and (Z)-1-Chloro-4-[2-(4-methoxyphenyl)-1-phenoxyvinyl]benzene (**6ea'**) (**6ea/6ea'** = 1/0.24)*: According to the general procedure, a crude product, which was prepared from **4e**[161] (121.4 mg, 0.50 mmol), phenol (52.0 mg, 0.55 mmol) and [Au(IPr)]$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give the inseparable mixture of **6ea** and **6ea'** (**6ea** /**6ea** = 1/0.24, 158 mg, 94%, average of two runs) as a white solid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.63-7.44 (m, 4 + 0.96H), 7.32-7.16 (m, 4 + 0.96H), 7.01-6.90 (m, 3 + 0.72H), 6.89-6.77 (m, 2 + 0.48H), 6.61 (s, 0.24H), 6.49 (s, 1H), 3.78 (s, 3 + 0.72H). **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$) δ 160.0, 159.1, 156.3, 156.22, 150.18, 146.9, 134.8, 133.87, 133.6, 132.6, 131.7, 130.5, 130.0, 129.9, 129.8, 128.9, 128.7, 128.2, 127.6, 127.3, 127.1, 122.2, 116.9, 116.4, 116.2, 114.2, 113.8, 55.39, 55.35.

*(Z)-(2-Phenoxyprop-1-en-1-yl)benzene (**6fa**) and (Z)-(1-Phenoxyprop-1-en-1-yl)benzene (**6fa'**) (**6fa/6fa'** = 1/0.18):* According to the general procedure, a crude product, which was

prepared from 1-phenylpropyne (**4f**) (58.0 mg, 0.50 mmol), phenol (**5a**) (52.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 0.25 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 6 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give the inseparable mixture of **6fa** and **6fa'** (**6fa**/**6fa** = 1/0.18, 94 mg, 90%, average of two runs) as a colorless liquid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.58-7.43 (m, 2 + 0.36H), 7.40-7.11 (m, 5 + 0.90H), 7.11-6.90 (m, 3 + 0.84H), 5.94 (q, *J* = 7.1 Hz, 0.18H), 5.88 (s, 1H), 1.98 (s, 3H), 1.76 (d, *J* = 7.1 Hz, 0.54H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ157.4, 155.4, 149.7, 149.3, 135.6, 135.3, 129.7, 129.6, 128.6, 128.4, 128.2, 127.9, 126.6, 125.2, 122.8, 121.5, 117.7, 115.4, 115.0, 112.5, 19.7, 11.6.

*(Z)-1-Nitro-4-[(1-phenylprop-1-en-2-yl)oxy]benzene (**6fg**) and (Z)-1-Nitro-4-[(1-phenylprop-1-en-1-yl)oxy]benzene (**6fg'**) (**6fg** /**6fg'** = 1/0.35):* According to the general procedure, a crude product, which was prepared from 1-phenylpropyne (**4f**) (58.0 mg, 0.50 mmol), 4-nitrophenol (**5g**) (77.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 90/10) to give the inseparable mixture of **6fg** and **6fg'** (**6fg**/**6fg'** = 1/0.35, 115 mg, 90%, average of two runs) as a colorless liquid, whose NMR data were consistent to those reported in the literature.[153] **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.27-8.11 (m, 2 + 0.70H), 7.48-7.35 (m, 2 + 0.70H), 7.35-7.13 (m, 3 + 1.05H), 7.13-6.98 (m, 2 + 0.70H), 6.07 (q, *J* = 0.9 Hz, 0.35H), 6.03 (q, *J* = 7.0 Hz, 1H), 2.05 (d, *J* = 0.9 Hz, 3H), 1.75 (d, *J* = 7.0 Hz, 1.05 H). **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$) δ 162.5, 160.7, 149.2, 147.5, 142.7, 142.2, 134.3, 134.1, 128.8, 128.6, 128.5, 128.3, 127.3, 126.14, 126.13, 124.9, 117.5, 116.5, 115.6, 113.3, 19.8, 11.5.

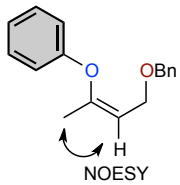
*(Z)-2-(2-Phenoxyhex-1-en-1-yl)pyridine (**6ga**):* According to the general procedure, a crude product, which was prepared from **4g**[162] (79.6 mg, 0.50 mmol), phenol (5a) (52.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 72 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1~3/1) to give **6ga** (79 mg, 62%, average of two runs) as a colorless liquid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.44 (brs, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.42 (ddd, 8.0, 8.0, 1.8 Hz, 1H), 7.28-7.19 (m, 2H), 7.01-6.88 (m, 4H), 6.13 (s, 1H), 2.23 (t, *J* = 7.6 Hz, 2H), 1.46 (tt, *J* = 7.6, 7.6 Hz, 2H), 1.27 (tq, *J* = 7.6, 7.6 Hz, 3H), 0.80 (t, *J* = 7.6 Hz, 3 H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 156.6, 155.1, 154.6, 149.0, 136.4, 129.8, 123.2, 122.9, 121.2, 117.6, 116.1, 32.8, 29.2, 22.1, 13.9. **HRMS** (APCI) calcd for $C_{17}H_{20}NO$ [$(M+H)^+$] 254.1539, found 254.1540.



*(Z)-2-(2-Phenoxy-2-phenylvinyl)pyridine (**6ha**):* According to the general procedure, a crude product, which was prepared from **4h**[162] (89.6 mg, 0.50 mmol), phenol (**5a**) (52.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (6.5 mg, 0.5 μmol, 1.0 mol%) in toluene (1 mL) at 110 °C for 72 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1~3/1) to give **6ha** (46 mg, 34%, average of two runs) as a white solid. **^{1}H NMR** (CD_3OD, 300 MHz) δ 8.47 (d, *J* = 4.6 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.75-7.55 (m, 3H), 7.38-7.28 (m, 3H), 7.26-7.14 (m, 3H), 7.04-6.87 (m, 3H), 6.83 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, MeOD-d_4) δ 157.3, 155.0, 154.9, 149.7, 138.5, 136.4, 130.8, 130.4, 129.8, 127.6, 125.0, 123.6, 123.4, 117.4, 117.0. **HRMS** (APCI) calcd for $C_{19}H_{16}NO$ [$(M+H)^+$] 274.1226, found 274.1228.

*(Z)-3-(2-phenoxyhex-1-en-1-yl)pyridine (**6mt**) and (Z)-3-(1-phenoxyhex-1-en-1-yl)pyridine (**6mt'**) (**6mt/6mt'** =1/0.43):* According to the general procedure, a crude product, which was prepared from **4i**[162] (79.0 mg, 0.50 mmol), phenol (**5t**) (47.0 mg, 0.50 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (19.5 mg, 15 μmol, 3.0 mol%) in toluene (1 mL) at 110 °C for 16 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5~70/30) to give **6mt** and **6mt'** (**6mt** /**6mt'** = 1/0.43, 96 mg, 76%, average of two runs) as a pale yellow oil. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.77 (d, *J* = 1.8 Hz, 1H), 8.63 (br, 2.25H), 8.45 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.36 (d, *J* = 3.7 Hz, 2.33H), 7.94 (dt, *J* = 8.1, 1.9 Hz, 2.36H), 7.71 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.34-7.12 (m, 12H), 7.08-6.92 (m, 10H), 5.95-5.89 (m, 1 + 2.21H), 2.33-2.20 (m, 6.62H), 1.58-1.21 (m, 15.38H), 0.89 (t, *J* = 7.3 Hz, 10.38H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 157.0, 155.7, 155.1, 149.7, 148.8, 147.5, 147.1, 146.4, 134.9, 132.6, 131.3, 129.8, 129.8, 123.5, 123.3, 122.9, 121.9, 120.4, 117.4, 115.6, 111.2, 32.9, 31.4, 29.3, 25.7, 22.6, 22.2, 14.0, 14.0. **HRMS** (ESI) calcd for $C_{17}H_{20}O_1N_1$ [$(M+H)^+$] 254.1539, found 254.1541.

*(Z)-[{4-(benzyloxy)but-2-en-2-yl}oxy]benzene (**6ja**)*: According to the general procedure, a crude product, which was prepared from alkyne **4j**[163] (160.0 mg, 1.00 mmol), phenol (**6a**) (47.0 mg, 0.50 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 2.5 μmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ja** (89 mg, 70%, average of two runs) as a colorless liquid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.34-7.18 (m, 7H), 7.03-6.94 (m, 1H), 6.94-6.86 (m, 2 H), 5.21 (t, *J* = 6.8 Hz, 1H), 4.43 (s, 2H), 4.06 (d, *J* = 6.8 Hz, 2H), 1.81 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 101 MHz) δ 156.1, 150.9, 138.6, 129.7, 128.4, 127.9, 127.6, 122.4, 117.0, 112.6, 72.4, 64.5, 18.6; **HRMS** (APCI) calcd for $C_{17}H_{19}O_2$ [$(M+H)^+$] 255.1380, found 255.1375.



*(Z)-[{5-(benzyloxy)pent-2-en-2-yl}oxy]benzene (**6ka**) and (Z)-[{5-(benzyloxy)pent-2-en-3-yl}oxy]benzene (**6ka'**) (**6ka/6ka'** =1/0.17)*: According to the general procedure, a crude product, which was prepared from alkyne **4k**[164] (87.0 mg, 0.50 mmol), phenol (**5a**) (52.0 mg, 0.55 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] (3.2 mg, 2.5 µmol, 0.5 mol%) in toluene (1 mL) at 80 °C for 3 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **6ka** and **6ka'** (**6ka**/**6ka'** = 1/0.17, 114 mg, 85%, average of two runs) as a colorless liquid. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.33-7.14 (m, 7 + 1.19H), 6.96-6.80 (m, 3 + 0.51H), 5.12 (q, *J* = 6.7 Hz, 0.17 H), 5.03 (tq, *J* = 7.2, 1.1 Hz, 1H), 4.43 (s, 2H), 4.42 (s, 0.34H), 3.51 (t, *J* = 6.7 Hz, 0.34H), 3.41 (t, *J* = 7.2 Hz, 2H), 2.45-2.36 (m, 0.34H), 2.31 (dtq, *J* = 7.2, 7.2 1.1 Hz, 2H), 1.75 (dt, *J* = 7.2, 1.1 Hz, 3H), 1.50-1.47 (m, 0.51H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 75 MHz) δ 156.6, 156.4, 148.6, 148.4, 138.7, 138.5, 129.6, 129.6, 128.5, 128.4, 127.8, 127.8, 127.7, 127.6, 121.8, 121.6, 116.4, 115.9, 112.7, 112.3, 73.0, 72.8, 69.8, 67.5, 33.5, 26.0, 18.5, 10.9.

Catalyst Recycling Experiment: **1A** (3.2 mg, 2.5 µmol) was added to a solution of 4a (89 mg, 0.5 mmol) and **5a** (52 mg, 0.55 mmol) in toluene. The mixture was stirred at 80 ºC for 1 h. An aliquot of the reaction mixture was then examined by GC revealing 96% conversion to **6aa**. Afterwards, iterative additions of **4a** (0.5 mmol) and **5a** (0.55 mmol) were added to the reaction mixture. This process was repeated until 8.5 mmol of **4a** were converted to **6aa**, affording a TON of 3400.

Catalytic Studies Table 4, General procedure: [Au] (0.5-1 mol%) was added to a solution of alkyne (0.5 mmol) and phenol (0.55 mmol, 1.1 equiv) in toluene (1 mL). The reaction mixture was stirred at 80 °C for 60 min and an aliquot analysed by GC. The conversions are an average of at least two runs.

Catalyst Counter-ion effect, Figure 2: [{Au(NHC)}$_2$(µ-OH)][X], **1A-1Ad**, (X = BF_4, FABA, SbF_6, OTf and NTf_2; 2.5 µmol, 0.5 mol%) was added to a solution of alkyne (0.5 mmol) and phenol (0.55 mmol, 1.1 equiv) in toluene (1 mL). The reaction mixture was stirred at 80 °C for 60 min. Aliquots of the reaction media were taken at regular intervals and analysed by GC. The conversions are an average of at least two runs.

Table 5. Catalyst counter-ion effect

Time (min)	[Au][BF_4] (%)	[Au][OTf] (%)	[Au][NTf_2] (%)	[Au][SbF_6] (%)	[Au][FABA] (%)
2	12.00	4.32	1.42	7.12	14.83
5	24.25	7.84	0.65	16.41	29.89
10	44.50	16.77	1.65	28.32	51.15
15	59.00	23.33	1.62	42.35	65.67
20	72.00	28.74	2.22	54.85	80.59
25	80.00	34.13	1.85	63.65	87.63
30	84.75	39.23	2.47	71.66	93.32
35	90.00	41.77	3.09	77.26	95.46
40	90.00	43.84	3.26	82.53	96.93
45	93.67	46.97	2.59	81.56	97.17
50	94.00	55.05	4.08	90.60	98.23
55	-	57.13	3.13	88.83	98.98
60	97.25	60.09	5.79	94.17	99.00

*Synthesis of [Au(IPr)(η^2-Ph-C≡C-Ph)][BF_4] (**IA**)*: $AgBF_4$ (94 mg, 0.483 mmol) was added to a stirred solution of [Au(IPr)Cl] (300 mg, 0.483 mmol) and diphenylacetylene (**4a**) (86.0 mg, 0.483 mmol) in dichloromethane (3 mL). The mixture was stirred at room temperature for 30 min in the absence of light. The crude mixture was filtered through a pad of Celite® and washed with dichloromethane (~ 4 mL). The solvent was reduced under vacuum and the product precipitated by addition of pentane. **IA** was obtained as a white solid in 73% yield (300 mg, 0.353 mmol). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.66 (t, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.52-7.48 (m, 4H, CH_{imid} + C$H_{p\text{-}Ph}$), 7.36 (d, *J* = 7.8 Hz, 4H, CH_{Ar}), 7.30-7.26 (m, 4H, C$H_{m\text{-}Ph}$), 6.93-6.91 (m, 4H, C$H_{o\text{-}Ph}$), 2.50 (sept, *J* = 6.9 Hz, 4H, C$H_{i\text{Pr}}$), 1.25 (d, *J* = 6.8 Hz, 12H, CH_3), 1.14 (d, *J* = 6.9 Hz, 12H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ 176.2 (C_{carb}), 146.3 (C_{Ar}), 133.3 (C_{Ar}), 132.33 ($CH_{p\text{-}Ph}$), 132.27 ($CH_{o\text{-}Ph}$), 132.0 (CH_{Ar}), 129.8 ($CH_{m\text{-}Ph}$), 125.6 (CH_{imid}), 125.1 (CH_{Ar}), 117.5 (C_{Ph}), 89.8 ($C_{acetylene}$), 29.3 ($CH_{i\text{Pr}}$), 24.7 (CH_3), 24.2 (CH_3). **Anal. Calcd.** for $C_{41}H_{46}AuBF_4N_2$ (850.34): C, 57.89%; H, 5.45; N, 3.29. Found: C, 57.92%; H, 5.55; N, 3.33.

*Synthesis of [Au(IPr)(OPh)] (**IIA**)*: [Au(IPr)OH] (**3A**) (73 mg, 121 μmol) and phenol (**5a**) (12 mg, 121 μmol) were dissolved in dichloromethane (2 mL). The solution was heated to 50 ºC and stirred for 2 hours. The reaction mixture was allowed to cool and filtered trough a pad of aluminium oxide. The solvent was reduced under vacuum and the product precipitated by addition of pentane. After filtration, **IIA** was obtained as a white solid in 64% yield (53 mg, 78 μmol). **^{1}H NMR** (300 MHz; CD_2Cl_2): 7.55 (t, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.37 (d, *J* = 7.8, 4H, CH_{Ar}), 7.27 (s, 2H, CH_{imid}), 6.79 (m, 2H, C$H_{m\text{-phenoxide}}$), 6.36 (m, 1H, C$H_{p\text{-phenoxide}}$), 6.22 (m, 2H, C$H_{o\text{-phenoxide}}$), 2.61 (sept, *J* = 6.9 Hz, 4H, C$H_{i\text{Pr}}$), 1.35 (d, *J* = 6.9 Hz, 12H, CH_3), 1.24 (d, *J* = 6.9 Hz, 12H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ 169.6 (C_{carb}), 168.5 ($C_{phenoxide}$),

146.3 (C_{Ar}), 134.7 (C_{Ar}), 131.0 (C_{Ar}), 128.7 ($CH_{m\text{-phenoxide}}$), 124.6 (CH_{Ar}), 123.7 (CH_{imid}), 118.5 ($CH_{o\text{-phenoxide}}$), 114.7 ($CH_{p\text{-phenoxide}}$), 29.2 ($CH_{i\text{Pr}}$), 24.46 (CH_3), 24.26 (CH_3). **Anal. Calcd.** for $C_{33}H_{41}AuN_2O$ (678.29): C, 58.40%; H, 6.09%; N, 4.13%. Found: C, 58.35%; H, 6.12%; N, 4.20%.

Synthesis of [{Au(IPr)}$_2$(μ-OPh)][BF$_4$] (V): In a glovebox under an Ar atmosphere, **5a** (5 mg, 53 μmol) was dissolved in dry CH_2Cl_2 (1 mL) in the presence of 4 Å molecular sieves, and stirred for 3 h at room temperature. Then **1A** (60 mg, 47 μmol) was added and the reaction mixture stirred for another 3 h at room temperature. The solution was then filtered through a pad of oven dried cotton, to remove residues from the molecular sieves, reduced under vacuum to ~ 0.1 mL, the product precipitated by addition of dry pentane (~ 3 mL) and finally, after decantation the supernatant was removed. The solid was washed again with pentane (2 x 3 mL) to remove the excess of **5a**. After drying under high vacuum, digold [{Au(IPr)}$_2$(μ-OPh)][BF$_4$] (**V**) was obtained as a white solid in 78% yield (50 mg, 37 μmol). **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.59 (t, J = 7.8 Hz, 4H, CH_{Ar}), 7.30 (d, J = 7.8 Hz, 8H, CH_{Ar}), 7.27 (s, 4H, CH_{imid}), 6.68-6.66 (m, 3H, $CH_{m\text{-phenoxide}}$ + $CH_{p\text{-phenoxide}}$), 5.93-5.91 (m, 2H, $CH_{o\text{-phenoxide}}$), 2.40 (sept, J = 6.7 Hz, 8H, $CH_{i\text{Pr}}$), 1.19 (d, J = 6.9 Hz, 24H, CH_3), 1.06 (d, J = 6.8 Hz, 24H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ 163.7 ($C_{phenoxide}$), 161.5 (C_{carb}), 146.0 (C_{Ar}), 134.0 (C_{Ar}), 131.3 (C_{Ar}), 129.0 ($CH_{m\text{-phenoxide}}$), 124.79 (CH_{Ar}), 124.66 (CH_{imid}), 120.6 ($CH_{p\text{-phenoxide}}$), 118.3 ($CH_{o\text{-phenoxide}}$), 29.1 ($CH_{i\text{Pr}}$), 24.5 (CH_3), 24.0 (CH_3). **^{19}F{^{1}H} NMR** (282 MHz; CD_2Cl_2): δ -153.97, -154.02. **Anal. Calcd.** for $C_{60}H_{77}Au_2BF_4N_4O$ (1351.04): C, 53.34%; H, 5.74%; N, 4.15%. Found: C, 53.23%; H, 5.81%; N, 4.22%.

*Reactions between [Au(IPr)(η^2-Ph-C≡C-Ph)][BF$_4$] (**IA**) and phenol (**5a**), eq. 1 Scheme 8*:

- *Standard conditions:* **IA** (20 mg, 23.5 μmol) and **5a** (2.2 mg, 23.5 μmol) were dissolved in toluene and stirred at 80 ºC for 1 h. The solvent was then evaporated and the crude dissolved in CD_2Cl_2. ^{1}H NMR spectra showed a mixture between **IA** and [Au(IPr)$_2$][BF$_4$]. ~ 38% conversion towards the desired product **6aa** can also be observed.
- *Anhydrous conditions:* **IA** (20 mg, 23.5 μmol) and **5a** (2.2 mg, 23.5 μmol) were dissolved in dry CD_2Cl_2 under an argon atmosphere at room temperature. After 4 h no reaction could be observed. After 16 h, 8% conversion to **6aa** can be observed and after 3 d it increases to 21%.

This series of experiments show that the addition of phenols to alkynes can be catalysed by cationic gold species alone, but the reaction is too slow to be efficient.

*Reaction between [Au(IPr)(OPh)] (**IIA**) and diphenylacetylene (**4a**), eq. 2 Scheme 8*:

- *Standard conditions*: **IIA** (20 mg, 29.5 µmol) and **4a** (5.3 mg, 29.5 µmol) were dissolved in toluene and stirred at 80 ºC for 1 h. **IIA** was not soluble in the reaction media. After 1 h, the solvent was evaporated and the crude dissolved in CD_2Cl_2. ^1H NMR spectra showed no reaction.
- *Anhydrous conditions*: **IIA** (20 mg, 29.5 µmol) and **4a** (5.3 mg, 29.5 µmol) were dissolved in dry CD_2Cl_2 under an argon atmosphere at room temperature. No reaction could be observed after 3 d.

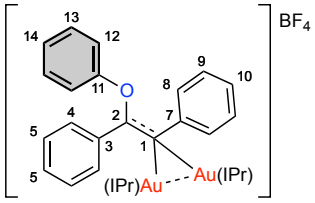
These experiments show that the addition of phenols to alkynes cannot be catalysed by **II** alone.

*Reaction between [Au(IPr)(η^2-Ph-C≡C-Ph)][BF_4] (**IA**) and [Au(IPr)(OPh)] (**IIA**), Scheme 9:*

- *Standard conditions*: **IA** (20 mg, 23.5 µmol) and **IIA** (16 mg, 23.5 µmol) were dissolved in toluene and stirred at 80 ºC for 1 h. Not everything was soluble in the reaction media. After 1 h, the solvent was evaporated and the crude dissolved in CD_2Cl_2. ^1H NMR spectra showed a complex mixture where none of the starting materials can be observed. The only identified species in this mixture are **1A** and product **6aa**. Unfortunately, due to the complexity of the mixture conversions cannot be determined.
- *Room temperature, under air, non-dried solvents*: **IA** (20 mg, 23.5 µmol) and **IIA** (16 mg, 23.5 µmol) were dissolved in CD_2Cl_2 (0.6 mL) and stirred at room temperature. After 5 min none of the starting materials can be observed by ^1H NMR. Traces of **6aa** and formation of **1A** can be observed. After 2 d at room temperature, **6aa** and **1A** are the main species in the media.
- *Anhydrous conditions:* **IA** (20 mg, 23.5 µmol) and **IIA** (16 mg, 23.5 µmol) were dissolved in dry CD_2Cl_2 (0.6 mL) under argon atmosphere and stirred at room temperature. After 5 min none of the starting materials can be observed by ^1H NMR. A complex mixture of at least two new aurated species can be observed. One of them was identified as digold complex **V**. We proposed that the other could be *gem*-diaurated intermediate **III** and that the mixture that we observed is in fact an equilibrium between **V**, **4a** and **III** (Scheme 8). To prove this hypothesis **4a** (5 mg, 28 µmol) was added to the mixture and stirred for 10 min. The ^1H NMR of the reaction mixture showed complete conversion to *gem*-diaurated species **III** (Figure 4). The solution was reduced under vacuum to ~ 0.1 mL, the product was precipitated by addition of dry pentane (~ 3 mL) and finally, after decantation the supernatant was removed. The solid was washed again with pentane (2 x 3 mL) to remove the excess

of **4a**. After drying under high vacuum the solid was analysed by ^{1}H NMR showing a mixture of **V**, **4a** and **III** (Figure 3). This result suggests that we were in the presence of a reversible process and that *gem*-diaurated species **III** could not be isolated. Therefore, this species was characterised in the reaction mixture.

*Characterisation of gem-diaurated species **III**:* **^{1}H NMR** (400 MHz; CD_2Cl_2): δ 7.48 (t, *J*



= 7.8 Hz, 4H, CH_{Ar}), 7.23 (m, 2H, CH^{4}), 7.19 (d, *J* = 7.8 Hz, 8H, CH_{Ar}), 7.16 (s, 4H, CH_{imid}), 7.05-7.01 (m, 2H, CH^{13}), 6.98-6.92 (m, 1H, CH^{6}), 6.84 (m, 2H, CH^{10} + CH^{14}), 6.66-6.62 (m, 2H, CH^{9}), 6.56-6.52 (m, 2H, CH^{5}), 6.51-6.48 (m, 4H, CH^{8} + CH^{12}), 2.52-2.39 (m, 8H, C$H_{i\mathrm{Pr}}$), 1.10 (d, *J* = 6.9 Hz, 24H, CH_3), 1.01 (d, *J* = 6.2 Hz, 24H, CH_3). **^{13}C{^{1}H} NMR** (101 MHz; CD_2Cl_2): δ 181.9 (C_{carb}), 172.8 (C^{2}), 157.3 (C^{11}), 145.5 (C_{Ar}), 143.0 (C^{7}), 135.0 (C^{3}), 134.5 (C_{Ar}), 131.2 (CH_{Ar}), 130.0 (CH^{6}), 129.5 (CH^{13}), 129.3 (CH^{8}), 128.5 (CH^{5}), 128.10 (CH^{4}), 128.06 (CH^{9}), 126.0 (CH^{10}), 124.90 (CH_{imid}), 124.84 (CH_{Ar}), 123.0 (C^{1}), 122.5 (CH^{14}), 117.43 (CH^{12}), 29.0 ($CH_{i\mathrm{Pr}}$), 24.7 (CH_3), 24.2 (CH_3). **^{19}F{^{1}H} NMR** (376 MHz; CD_2Cl_2): δ -153.85, -153.90.

Conclusions

The initial aims of this project were simple, to study the reactivity of Au-NHC complexes in homogeneous catalysis. However, during the synthesis of [Au(IPr*)Cl] we realised that there was a lack of a general, robust protocol for the synthesis of [Au(NHC)Cl] species. Therefore, a new synthetic approach was envisioned and through a thorough optimisation of the reaction conditions we were able to develop an eco-friendly, multi-gram scale process for the synthesis of [Au(NHC)X] (X = Cl, Br, I) complexes.

Interested by the reactivity displayed by the golden synthon [Au(IPr)(OH)] we wondered whether it would be possible to synthesise a series of [Au(NHC)(OH)] complexes. Unfortunately, the reported protocol for the synthesis of [Au(IPr)(OH)] was not suitable for other type of NHCs. Therefore, a new procedure was devised that allowed access to [Au(NHC)(OH)] (NHC = SIPr, IPr^{Cl}, IPr^{Me}, IPr* or IPr^{*-Tol}). Moreover, our investigations suggest that the steric hindrance around the metal centre plays a crucial role on the stabilisation of Au-hydroxide species and it is the reason why gold hydroxides bearing bulky NHC ligands are stable while complexes bearing smaller NHCs are not.

Since silver salts are hygroscopic, expensive, light sensitive and can display catalytic activity, chemists are starting to develop silver-free protocols for gold catalysis. We have contributed to this field with the synthesis of a library of digold hydroxides, $[\{Au(NHC)\}_2(\mu\text{-}OH)][BF_4]$ (NHC = SIPr, IPr^{Cl}, IPr* or IPent), and their application as silver-free catalysts in a series of gold-catalysed water-inclusive transformations such as alkyne and nitrile hydration and Meyer-Schuster rearrangement.

Moreover, we have been able to use digold hydroxide $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ to access key diaurated intermediates in gold-catalysed transformations. Using $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ we have been able to develop the first straightforward protocol for the synthesis of gem-diaurated and σ,π-digold-acetylide species bearing NHCs as ancillary ligands.

Finally, taking advantage of the bifunctional nature of digold hydroxides, which can act as Lewis acids and Brønsted bases, we have been able to develop a highly efficient protocol for the synthesis of vinyl ether derivatives. Moreover, this gold-catalysed process constitutes, to the best of our knowledge, the first catalysed reaction were *two* gold centres interact with *two* independent substrate molecules.

The work presented in this thesis represents a significant contribution towards the robust and reproducible synthesis of important complexes in gold catalysis using NHC as ancillary ligands. Future work in this area in the Nolan group is already underway, with additional catalytic applications and synthetic organometallic chemistry being explored.

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