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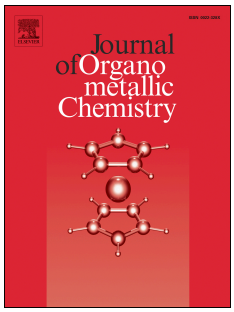

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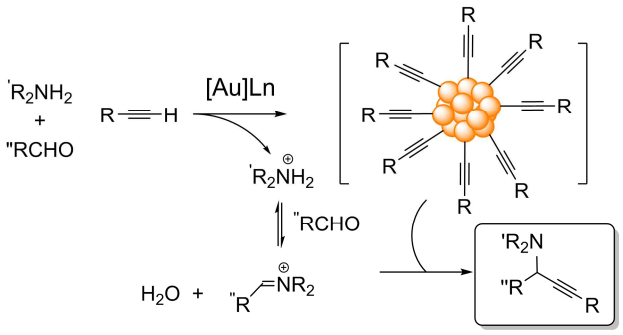

Some Insights into the Gold-Catalysed A^3-Coupling Reaction

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Abstract. A series of cyclometallated and functionalised NHC gold(I) and gold(III) complexes, many of which feature chiral ligands, and their application to A^3-coupling reactions is presented. Gold(III) complexes were found to be particularly effective catalysts for the coupling in a range of solvents, however no asymmetric induction was obtained when using chiral gold complexes and the rate of product formation was found to be similar even when using different ligand systems. In-situ NMR analysis of these reactions indicates that decomposition of the catalyst occurs during the course of the reaction while TEM studies revealed the presence of gold nanoparticles in crude reaction mixtures. Taken together these data suggest that the gold nanoparticales, rather than the intact gold complexes, could be the catalytically active species, and if so this may have significant implications for other gold-catalysed systems.

Dedicated to Dr. Mark Whiteley (an outstanding colleague) on his retirement from the School of Chemistry, University of Manchester.

Introduction

A major theme in contemporary chemical research is concerned with the discovery of reactions which facilitate a rapid increase in chemical complexity and the development of cleaner, more efficient chemical processes, especially as applied to the pharmaceutical and fine chemicals industries.[1–5] In this context the resurgent use of coinage metals as catalysts in organic synthesis has received much attention, and has resulted in the development of a wide range of gold-catalysed reactions.[6–11] Even though in many cases the nature of the active catalytic species involved in these transformations has yet to be resolved, as has a full description of the mechanistic pathways of the reactions concerned.[12,13] Despite the ever burgeoning literature concerning gold-catalysed reactions, the majority of structurally defined chiral gold complexes are restricted to those bearing chiral phosphane ligands.[14–19]

Given the fact the use of gold-NHC complexes[20-26] is now *de rigour* in synthesis, it is somewhat surprising that reports of structurally characterised, chiral, Au(I)-NHC[27-36] and Au(I)-ADC/NAC[37] complexes are still comparatively scarce. Likewise, the synthesis and characterisation and catalytic activity of cyclometallated gold(III) complexes is relatively unexplored, with only a handful of examples being cited in the literature.[38]

As part of a broader, and continuing, investigation into the coordination chemistry of gold complexes with novel ligand systems[39,40] and the use of transition metals in organic synthesis we have prepared a number of organogold complexes with a view to investigating their role in A^3 –coupling reactions – a multi-component process which leads to the preparation of synthetically useful propargylamines.[41] Herein we present our findings concerning the development of an operationally simple route to chiral cyclometallated Au(III) complexes, the synthesis and structural characterisation of novel Au(I)-NHC complexes, together with an indication of their efficacy in A^3-coupling reactions.[42]

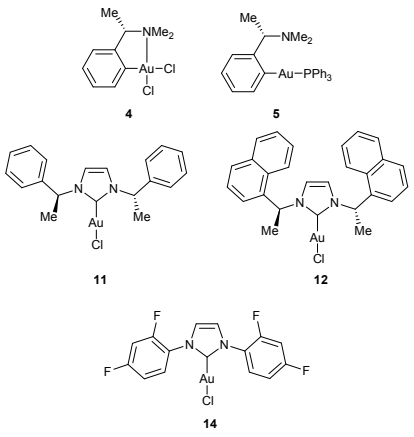
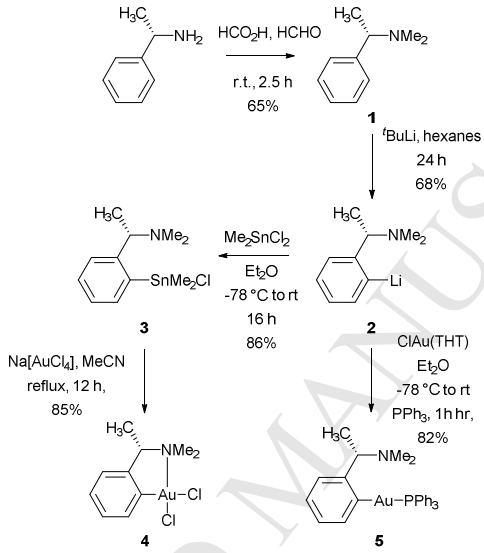


Figure 1: Gold complexes screened in A^3-coupling reactions

2. Results and Discussion

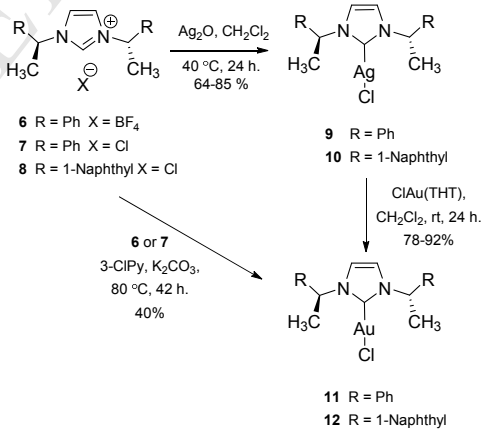
2.1 Synthesis of chiral gold complexes

The present study concerns the preparation, characterisation and subsequent estimation of the catalytic activity of the gold complexes presented in Figure 1. The chiral, cyclometallated, complex **4**, and **5** were prepared according to Scheme 1 starting from readily available[43] (*S*)-α-methyl-*N,N*- dimethylbenzylamine, **1**. Lithiation of **1** with ^{t}BuLi afforded isolable (*S*)-1-LiC_6H_4CH(Me)NMe_2[44] **2**, which was subsequently quenched with dichlorodimethylstannane to afford (*S*)-[$SnMe_2Cl(\eta^2$-*C,N*-C_6H_4CH(Me)NMe_2)] **3** in excellent yield. Transmetallation of **3** to either a gold(III) or **2** to a gold(I) centre was readily achieved affording (*S*)-[$AuCl_2(\eta^2$-*C,N*-C_6H_4CH(Me)NMe_2)] **4** or (*S*)-[$Au(PPh_3)(\eta^1$-C_6H_4CH(Me)NMe_2)] **5**. Both **4** and **5** are colourless, crystalline, solids and appear to be stable indefinitely when stored at ambient temperature, although **4** is slightly light sensitive and so was stored away from direct sunlight.



Scheme 1: Preparation of compounds **1**-**5**.

The chiral imidazolium salts **6**, **7** and **8** which were required for the preparation of the gold NHC complexes **11** and **12** were synthesised by the 'one-pot' procedures reported by Alexakis et al.[45] and Hermann and co-workers (Scheme 2).[46] Hence, reaction of either (*S*)-(-)-α-methylbenzylamine or (*S*)-(-)-1-(1-naphthyl)ethylamine with glyoxal and paraformaldehyde in the presence of either HCl or HBF_4 at 40 °C in toluene overnight afforded the desired salts. We assume that, based upon literature precedent,[32] the synthesis of the imidazolium salts **6**, **7** and **8** and subsequent conversion into **11** and **12** proceeds without racemization, an outcome which is in keeping with subsequent X-ray analysis of **11** and **12**.[1]



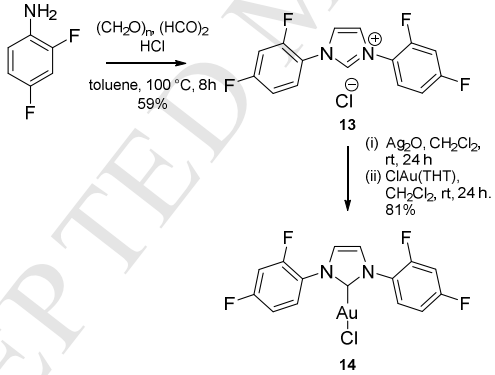
Scheme 2: Preparation of chiral NHC precatalysts.

[1] In addition, epimerisation of the chiral centres α-to *N* during these transformations would most probably generate diastereoisomeric mixtures of complexes which would be detected in the ^{1}H and ^{13}C NMR spectra of these products.

Reaction of the imidazolium chlorides **7** and **8** with Ag_2O, following the procedure reported by Alexakis *et al*,[45] cleanly afforded the Ag(I) complexes 1,3-bis-(1(*S*)-1-phenyl-ethyl)-imidazolin-2-ylidene silver chloride **9** and 1,3-bis-(1(*S*)-1-naphthyl-ethyl)-imidazolin-2-ylidene silver chloride **10** respectively. Finally, transmetallation from Ag(I)-NHC complexes to a gold(I) centre was effected by reaction of these complexes with ClAu(THT)[47] (where THT = tetrahydrothiophene),[48] and afforded analytically pure samples of **11** and **12** after a single recrystallisation from CH_2Cl_2/hexane. The carbene complex **11** could also be prepared directly from either of the imidazolium salts **6** and **7** using the method recently reported by Zhu and coworkers.[49] However, while mild thermolysis of a slurry of the respective immidazolium salt, K_2CO_3 and ClAu(THT) in 3-chloropyridine at 90 °C did afford the desired gold(I) complex **11**, the product yields afforded by this direct process were substantially reduced (*ca*. 40%) when compared to the transmetallation route.[50]

The preparation of metal complexes containing fluorine-substituted NHC ligands is of current interest due to the electronic and steric effects that a fluorine substituent may exert on the properties of the ligand or structure of the resulting complex.[51-55] In the context of the present study we wished to introduce a fluorine tag into the ligand system in order to probe the fate of gold catalysts or pre-catalyst during A^3-coupling reactions. Fortuitously Hope and coworkers[56] recently reported the synthesis of fluoroaryl-substituted imidazolium and iridium NHC complexes *via* the imidazolium salt **13**. We envisaged that **13** could be employed in the preparation of the fluorinated-NHC gold(I) complex **14** thereby enabling the course of A^3 reactions to be followed using ^{19}F NMR spectroscopy.

The synthesis of gold(I)-NHC complex **14** followed the standard route for **9** and **10**, utilising a transmetallation step, as depicted in scheme 3. Thus, metallation of **13** (Ag_2O, in CH_2Cl_2, rt) followed by *in-situ* transmetallation with ClAu(THT) afforded **14** as an air-stable solid in excellent overall yield (81%). Disappointingly, the direct route to **14**, involving heating **13** at 80 °C with $K[AuCl_4]$ and K_2CO_3 in 3-chloropyridine did not yield the desired product.
All of the new gold complexes were fully characterised by elemental analysis (C, H and N) and NMR spectroscopy (^1H, $^{13}C\{^1H\}$), see ESI.[†] In addition for compounds **4**, **5**, **11**, **12** and **14** single crystals suitable for X-ray diffraction studies[◊] were obtained; see Figures 2-4 for ORTEP[57] representations of the complexes and selected bond lengths (Å) and bond angles (°). Complex **4** crystallised in the triclinic space group *P1*, with the gold(III) atom in a typical square planar arrangement with bond angles around the gold centre ranging from 80.5(12)° (C1-Au-N1) to 95.7(12)° (N1-Au-Cl2).



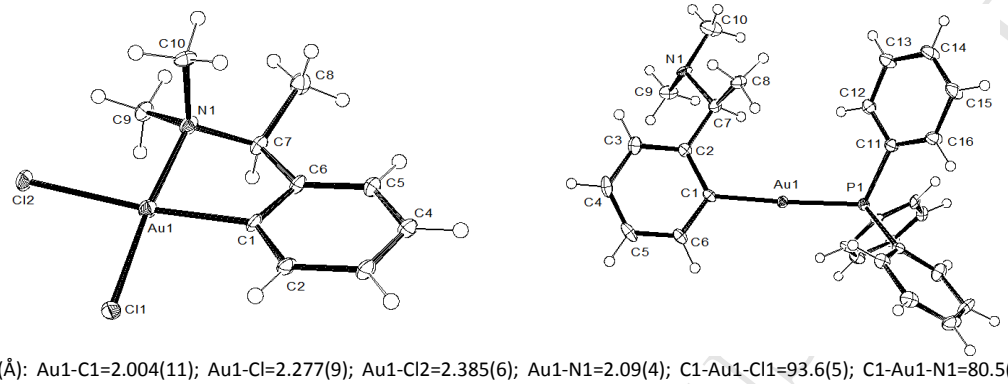
Scheme 3: Preparation of fluorinated gold NHC complex **14**.

By way of comparison, the related gold(I) complex **5** adopts a near-linear arrangement with a C1-Au1-P1 bond angle of 176.2(2)°. The Au1-C1 and Au1-P1 bond lengths of 2.0419(9) Å and 2.295(3) Å respectively are comparable to those previously reported for similar complexes.[58–61] Interestingly, as shown in figure 2, the amine moiety of **5** is rotated away from the Au(I) centre, presumably in order to minimise non-bonding interactions with the phosphane ligand, and therefore has no interaction with the metal atom (d(Au1…N1) = 4.662(7) Å, C1-C2-C7-N1 torsion angle of 152.7(8)°). This is in contrast to **4** (figure 2) which exists as a *C,N*-Au chelate (d(Au1-N1) = 2.09(4) Å, C1-C6-C7-N1 torsion angle of 29(3)°) with the nitrogen coordinated to the more Lewis-acidic Au(III) centre. Complex **11** crystallizes in the chiral space group *C121* with 3 gold molecules in the asymmetric unit and one molecule of toluene. The average Au1-C1 and Au1-Cl1 bond lengths of 1.985(9) Å and 2.289(2) Å respectively are comparable to those reported for other Au(I)-NHC complexes.[48,62–64] The average C1-Au1-Cl1 bond angle of 175.3(2)° confirms a near linear coordination geometry about the Au(I) centre. The *N*-substituents adopt an extended conformation, with the methyl-substituents *anti*-disposed with respect to each other about the central NHC-moiety.

Complex **12** crystallises in the monoclinic space group $P2_1$ and has two unique molecules in the asymmetric unit. The average Au1-C1 bond length of 1.976(18) Å and a C1-Au1-Cl1 bond angle of 177.9(6)° which again is in line with previously reported values for Au(I) N-heterocyclic carbene complexes. Complex **14** crystallizes in the monoclinic space group $P2_1/n$ with 4 molecules in the unit cell. The Au1-Cl1 bond length of 1.982(6) Å and C1-

Au1-Cl1 bond angle of 176.54(17)° is again typical of Au(I)-NHC complexes and there are no significant intramolecular Au-F interactions (d(Au1-F1) = 4.965(4) Å; d(Au1-F3) = 5.083(4) Å). The X-ray structure of **14** is shown in figure 4 and was found to be similar to that of the recently described[65] analogous dinitro-complex **15** (Figure 4) in the solid state. In particular the torsion angles about the N2 - C10 bond are comparable for both complexes (-124.5(6)° and -122.5(4)° respectively). In solution there is also no evidence for intramolecular F-Au interactions as judged by ^{19}F NMR spectroscopy[56] (^{19}F δ ($CDCl_3$) -105.0 ppm (d, $^4J_{FF}$= 8.3 Hz) and -117.9 ppm (d, $^4J_{FF}$= 8.3 Hz)) and the ^{13}C chemical shift for the carbene carbon (172.9 ppm) resonance is again typical of Au(I)-NHC complexes.

Figure 2: Molecular structures of complexes **4** and **5** showing the atomic numbering schemes, ellipsoids at 40%. **Complex 4:** Selected bond



lengths (Å): Au1-C1=2.004(11); Au1-Cl=2.277(9); Au1-Cl2=2.385(6); Au1-N1=2.09(4); C1-Au1-Cl1=93.6(5); C1-Au1-N1=80.5(12); Cl1-Au1-Cl2=90.2(3); N1-Au1-Cl2=95.7(12). Torsion angle (°): C1-C6-C7-N1=29(3). Displacement of N1 from Au1-C1-C6-C7 plane = 0.66(7) Å. **Complex 5:** Selected bond lengths (Å): Au1-P1=2.295(3); Au1-C1=2.041(9); Selected angles (°): P1-Au1-C1=176.2(2). Au1-N1 distance of 4.662(7) Å. Torsion angle (°) C1-C2-C7-N1=152.7(8).

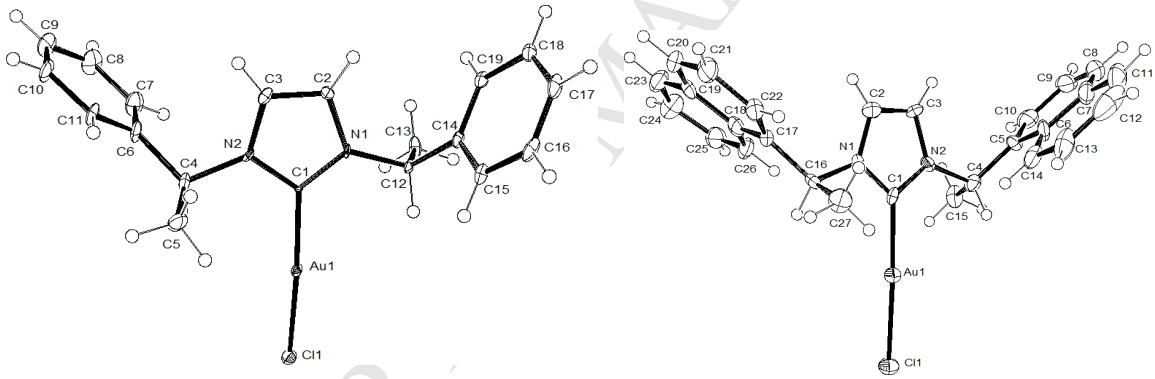
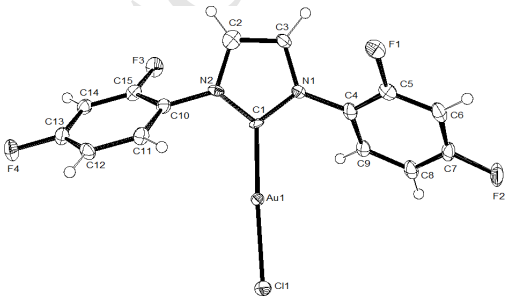
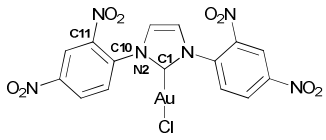


Figure 3: Molecular structure of residue 1 from **11** and residue 1 of **12** showing the atomic numbering scheme, ellipsoids at 40%. Toluene of crystallisation omitted for clarity. **Complex 11:** Selected bond lengths (Å): Au1-Cl1=2.285(2); Au1-C1=1.971(7); C1-N1=1.334(10); C1-N2=1.372(10); Selected angles (°): Cl1-Au1-C1=175.1(2); N1-C1-Au1=129.9(6); N1-C1-N2=104.2(6). Selected torsion angles (°): C5-C4-N2-C1=77.895(10); C13-C12-N1-C1=87.893(9). **Complex 12:** Selected bond lengths (Å):Au1-Cl1=2.278(4); Au1-C1=1.980(16); Selected angles (°): C1-Au1-Cl1=177.4(6). Selected torsion angles (°): C27-C16-N1-C1 = 71(2) °; C15-C4-N2-C1=85(2).



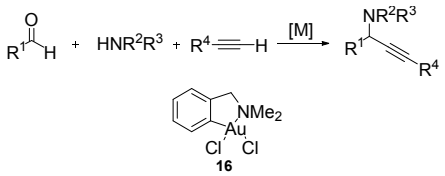


15

Figure 4: Molecular structure of complex 14 showing the atomic numbering scheme, ellipsoids at 40%. Selected bond lengths (Å): Au1-Cl1=2.2726(18); Au1-C1=1.971(7). Selected angles (°): Cl1-Au1-C1=176.8(2); N1-C1-N2=104.0(6). Torsion angles (°): C5-C4-N1-C1=−124.5(6); C15-C10-N2-C1=−125.5(7) Distances (Å): Au1-F1 = 4.965(4); Au1-F3 = 5.083(4). Selected data for complex 15[65]: Bond lengths (Å): Au-Cl =2.3000(9); Au-carbene C1 = 1.975(4). Torsion angle (°): C1-N2-C10-C11 = − 122.5(4).

2.2 Activity of complexes in A^3-coupling reactions

Having prepared a range of gold complexes their efficacy as catalysts in promoting the synthesis of propargylamines *via* the A^3-coupling reactions between an aldehyde, amine and alkyne was investigated (Scheme 4). In addition to the complexes described above, the achiral gold(III) complex [$AuCl_2(\eta^2$-*C,N*-$C_6H_4CH_2NMe_2)$] **16**, which was prepared by transmetallation from the precursor boroxine,[66] was also screened in the A^3-coupling reactions.



Scheme 4: Transition metal catalysed A^3-reaction.

Preliminary screening of **16** was performed by reacting benzaldehyde and phenylacetylene with a range of secondary amines, in water for 24 hours. Table 1 lists the data for a series of screening reactions. Excellent conversions and isolated yields were obtained for couplings with piperidine, pyrrolidine, morpholine and dibenzylamine (entries 1-4). Compound **4** was found to be an effective catalyst in all A^3-coupling reactions screened, with the conversions and yields obtained the same as those when **16** was employed as catalyst. However, complexes **5**, **11**, **12** and **14** were found to be much less effective (entry 4) under similar conditions, and required higher catalyst loadings and extended reaction times to effect conversion to the coupled product. It should also be noted that when the chiral complexes **4**, **5**, **11**, and **12**. were used in the general reaction depicted in Scheme 4, table 1 entry 4, there was no discernible enantiomeric enrichment as shown by HPLC, where baseline resolution of the two enantiomers showed that the reaction afforded a racemic mixture of products, see supplementary material.[67,68] In all other experiments separation of the enantiomers by analytical HPLC proved unsuccessful. In an effort to examine the scope of A^3-couplings catalysed by **16** and **4** various substrates were employed. First, chiral amine (*S*)-prolinol was found to react with benzaldehyde and phenylacetylene giving propargylamine in 56% yield (*d.r.* = 96:4; entry 5). This selectivity is comparable to that obtained previously with other cyclometallated gold(III) complexes.[37,38] The coupling of dibenzylamine, 3-trifluoromethylbenzaldehyde and phenylacetylene was found to proceed smoothly giving the CF_3-containing propargylamine in 80% yield (entry 6). Reaction of 2-formylpyridine with dibenzylamine and phenylacetylene resulted in the isolation of the rearranged aminoindolizine in 92% yield (entry 7), in a process analogous to that previously reported by Liu and Yan for the reaction catalysed by $Na[AuCl_4].2H_2O$.[69] A number of novel 'double A3'-coupling reactions using *bis*-aldehydes, *bis*-amines and *bis*-alkynes were also investigated in order to establish whether complexes **16** and **4** would facilitate coupling reactions with more challenging substrates. We observed that both terephthalaldehyde and *iso*phthalaldehyde underwent smooth A^3-reaction with phenylacetylene (2.6 equivalents) and dibenzylamine (2.1 equivs.) and afforded the corresponding *bis*-propargylamines in excellent yields (entries 8 and 9). Piperazine, a cyclic diamine, reacted with benzaldehyde (2 equivalents) and phenylacetylene (3 equivalents) and afforded the *bis*-propargylamine in 85% isolated yield (entry 10). The A^3-coupling reaction could also be extended to *bis*-alkynes such that reaction between 1,3-diethynylbenzene, dibenzylamine and benzaldehyde, again afforded the desired *bis*-propargylic amine in good yield (entry 11). A novel double coupling between ferrocene-1,1'-dicarbaldehyde,[70] dibenzylamine and phenylacetylene (entry 12) proceeded in excellent yield (95%), affording the *bis*-amine as 1:1 mixture of diastereoisomers. Indeed, It should be noted that all the 'double A^3-reactions' (entries 8-12) investigated produced a 1:1 mixture of the two diastereomers (as a racemic modification). Unfortunately, attempts to separate these diastereomers by HPLC failed. The gold-catalysed three-component coupling of ketones has met with scant attention, however Ji et al. have reported the use of $AuBr_3$ in such reactions using solvent-free reaction conditions.[71] Similarly, we observed that attempted A^3-coupling between cyclohexanone, morpholine and phenylacetylene, using either **16** or **4** as catalysts, in water met with failure. However good conversions could be achieved (resulting in product yields of 60%) when a catalyst loading of 5 mol% was employed under solvent-free reaction conditions (entry 13). The use of NHC gold(I) complexes containing weakly coordinating counteranions, has been proposed as a way to overcome the low catalytic activity frequently observed with *N*-heterocyclic carbene gold(I) chloride complexes.[72-75] Given the low reactivity of naphthyl complex **12**, we wondered if exchange of the chloride ligand for the more weakly bound bis(trifluoromethanesulfonyl)imidate moiety would afford a NHC complex with an improved reactivity profile in A^3-couplings. To this end **12** was reacted with one equivalent of silver bis(trifluoromethanesulfonyl)imide in CH_2Cl_2, according to the general method outlined by Gagosz et al.,[75] to give the NHC gold(I) triflimide complex **17** (Scheme 5).

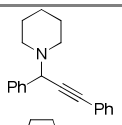
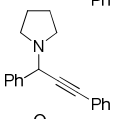
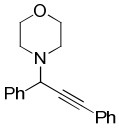
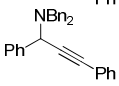
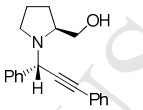
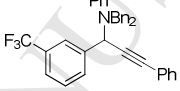
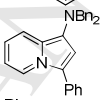
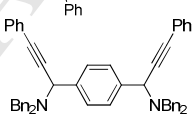
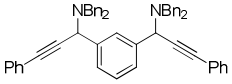
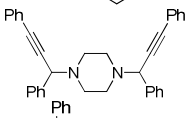
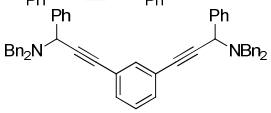
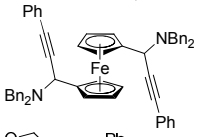
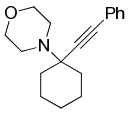
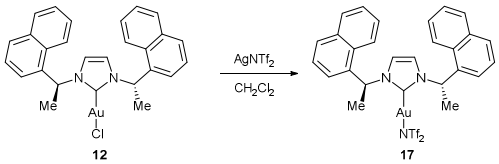
Entry	Aldehyde	Alkyne	Amine	Catalyst	Product	Conversion[b] (%)	Yield (%)
1	PhCHO	PhCCH	$C_5H_{10}NH$	4, 16		95, 95	75,75
2	PhCHO	PhCCH	C_4H_8NH	4, 16		92, 92	85,85
3	PhCHO	PhCCH	Morpholine	4, 16		90, 90	72,72
4	PhCHO	PhCCH	Bn_2NH	4, 16, 5[c], 11[d], 12[e], 14 16[g]		97[f], 97[f], 44[f], 9[f], 10[f], 9 9 (ee not determined)	85,85
5[h]	PhCHO	PhCCH	(***S***)-(+)-2-(CH_2OH)C_4H_7NH	4, 16		83, 83 (d.r 96:4)	55,55
6	3-(CF_3)-PhCHO	PhCCH	Bn_2NH	4, 16		98,98	80,80
7	C_5H_4N-2-CHO	PhCCH	Bn_2NH	4, 16		97,97	92,92
8[i]	1,4-(CHO)-C_6H_4	PhCCH	Bn_2NH	4, 16		98, 98	89,89
9[i]	1,3-(CHO)-C_6H_4	PhCCH	Bn_2NH	4, 16		98,98	85,85
10[i]	PhCHO	PhCCH	Piperazine	4, 16		95,95	85,85
11[i]	PhCHO	1,3-(HCC)-C_6H_4	Bn_2NH	4, 16		93,93	75,75
12[i]	Ferrocence-1,1'-dicarbaldehyde	PhCCH	Bn_2NH	4, 16		99,99	95,95
13[j]	Cyclo-C_6H_{10}(O)	PhCCH	morpholine	4, 16		-	60,60

Table 1: A^3-coupling reactions

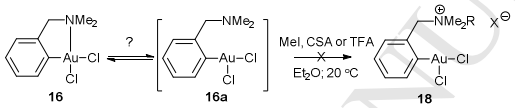
Reagents and conditions. [a] Standard reaction conditions: 1 mmol aldehyde, 1.1 mmol amine, 1.5 mmol alkyne, 2 mL H_2O, 40 ^oC, 24 h, 1 mol % catalyst; [b] conversion determined by ^1H NMR analysis of crude reaction mixtures based on aldehyde conversion); [c] when [(S)-Au(PPh_3)(η^1-$C_6H_4CH(Me)NMe_2$)] (**5**) is used as the catalyst the reaction is continued for 2 weeks at 40 ^oC.; [d] with 1,3-bis((*S*)-1'-phenylethyl) imidazolin-2-ylidene gold chloride (**11**) 2 mol% loading of complex and reaction continued for 168 h.; [e] with 1,3-bis((*S*)-1'-naphthylethyl) imidazolin-2-ylidene gold chloride (**12**) reaction contiunued for 72 h.; [f] enantiomeric excess found to be 0 %; [g] reaction conducted in the presence of **16** (1 mol%) and (-)-DIOP (1 mol%); [h] *d.r*. determined by ^1H NMR analysis of crude reaction mixture. With catalysts **4**, and **16** the d.r. is found to be 96:4; [i] reaction time increased to 48 h to give quantitative conversion. All 'double A^3' reactions give a 1:1 mixture of diastereomers which can be observed through some doubling of NMR signals; [j] 1.5 mmol cyclohexanone, 1 mmol morpholine, 1.5 mmol phenylacetylene, 5 mol % **4** or **16**, neat, 60 ^oC, 8 h.



Scheme 5: Synthesis of triflimide complex **17**.

Screening of **17** in the A^3-reaction between benzaldehyde, dibenzylamine and phenylacetylene resulted in a 15% conversion after 72 hours. This outcome is comparable to the conversion obtained when the parent chloride complex **12** is employed as catalyst (10% after 72 hours). To further examine the effect of varying the counterion 1 equivalent of silver triflate was added to the A^3-reaction catalysed by **12**. After 72 hours the conversion was <3%, indicating that substitution of a chloride ligand for triflimide or triflate has little effect on the catalytic activity of the NHC complex in this system.

Additionally, the stability of gold(III) complex **16** with respect to the generation of the unligated complex **16a**, an intermediate on a potential catalyst activation/decomposition pathway, was investigated by ^{1}H NMR spectroscopy (Scheme 6). Here, ^{1}H NMR analysis of the crude reaction mixtures derived from the reaction between **16** and an excess of either methyl iodide, camphorsulfonic acid or trifluoroacetic acid indicated that quaternisation of **16** to afford **18** had not occurred (see ESI for NMR spectra). This indicates that coordination of the NMe_2 group to the gold(III) centre in **16** is relatively strong and that the nitrogen atom is reasonably robust towards simple displacement, as has been previously documented.[76–78]



Scheme 6: Attempted quaternisation of complex **16**.

Next, the kinetics of the A^3-coupling reaction between benzaldehyde, dibenzylamine and phenylacetylene, in the presence of a series of gold catalysts, was investigated using ^{1}H NMR spectroscopy. Due to insolubility of the starting materials and product in D_2O the NMR experiments were performed in deuteroacetonitrile, which was found to be a reasonable substitute solvent. The relative activity of **16** was compared with $Na[AuCl_4]\bullet 2H_2O$ over a period of 12 h (Figure 5, **16**, ◆; $Na[AuCl_4]$, ■). Interestingly, for both **16** and $Na[AuCl_4]$ there appears to be no measurable induction period, at least on the NMR timescale, with product formation observed after *ca.* 5 min. In addition, the rate of product formation under these coupling conditions, appears to be equivalent within experimental error. Given that gold acetylide complexes are presumed to be the active catalytic species in A^3-

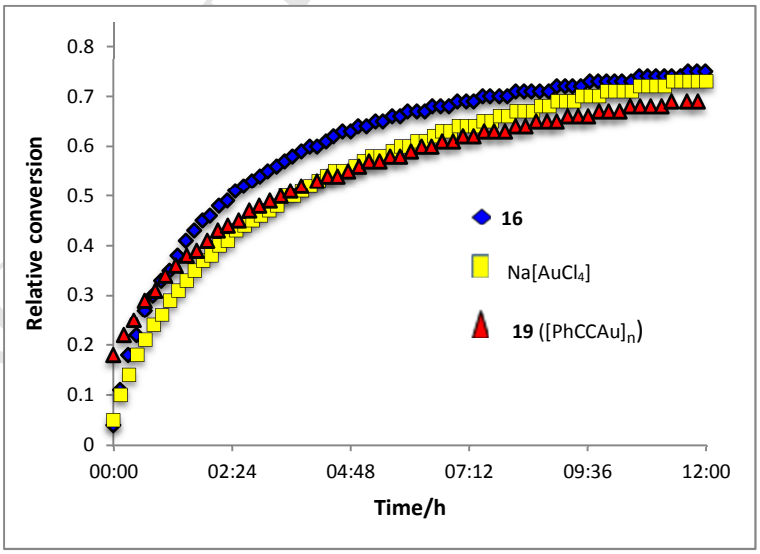
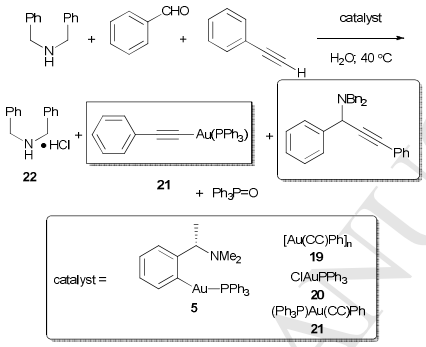


Figure 5: A plot of relative conversion versus time for A^3-coupling of benzaldehyde (1 mmol), dibenzylamine (1 mmol) and phenylacetylene (1.5 mmol), d^3-MeCN, 60 °C, 3 mol% Au catalyst.

reactions[42,79] we wondered if a common acetylide containing intermediate could have formed from both **16** and $Na[AuCl_4]$. To test this hypothesis the polymeric gold acetylide $[Au(CCPh)]_n$[80] (**19**) was synthesised and subsequently employed in A^3-coupling reactions. Despite the insolubility of complex **19** it was found to be an efficient catalyst for the coupling of benzaldehyde, dibenzylamine and phenylacetylene in H_2O (96% conversion in 24 h). Monitoring this reaction by ^1H NMR spectroscopy in deuteroacetonitrile (Figure 5, **19**) generated rate data that was complex (see ESI for details) but did however show that the initial rate of reaction was comparable to that observed for the reaction catalysed by either **16** or $Na[AuCl_4]$ (relative initial rates of 1:0.8:0.7 for **16**:Na[AuCl4]:**19**); once again no induction period could be detected. In addition analysis of the $^{31}P\{^1H\}$ NMR spectra of the crude reaction mixtures resulting from the A^3-reaction between benzaldehyde (1 mmol), dibenzylamine (1 mmol) which were promoted by the phosphane-containing catalysts $ClAuPPh_3$ (**20**), $(Ph_3P)Au(C{\equiv}CPh)$ (**21**), or (*S*)-$[Au(PPh_3)(\eta^1\text{-}C_6H_4CH(Me)NMe_2)]$ **5** in aqueous media all displayed resonances at *ca.* δ 42 ppm and 29 ppm, where the resonance at 42 ppm was assigned[81] to $(Ph_3P)Au(C{\equiv}CPh)$ (**21**) and that at δ 29 ppm corresponds to triphenylphosphine oxide ($Ph_3P{=}O$). Subsequent ^1H and $^{31}P\{^1H\}$ NMR experiments also indicated that the blank reaction between $ClAuPPh_3$ (**20**), piperidine and phenylacetylene, in the absence of benzaldehyde, also afforded the acetylide complex **21** and ammonium salt **22**, Scheme 7.



Scheme 7: Fate of phosphane-containing catalysts during A^3-coupling reactions.

In the case of the A^3-coupling reaction between benzaldehyde, dibenzylamine and phenylacetylene which were catalysed by **5** the formation of **21** and $Ph_3P{=}O$ was once again observed in the $^{31}P\{^1H\}$ NMR spectrum of the crude reaction mixture with concomitant disappearance of the co-ordinated phosphane resonance at δ 44.09 ppm for **5**. The loss of the chiral cyclometallated ligand in this case is presumably facilitated by the lack of coordination of the NMe_2 group to the gold centre and may provide an explanation as to the lack of asymmetric induction in this reaction. Significantly addition of triphenylphosphine, dppe or (-)-DIOP to the A^3-reactions catalysed by either $Na[AuCl_4].2H_2O$ or the chelated Au(III) complex **16** resulted in significant diminution in the rate of the A^3-reactions, (Table 2; Entries 5-7). Addition of 1 mol% of PPh_3 to these reactions resulted in a decrease in the degree of conversion from 100% to 77% and 31% under our standard reaction conditions (24 hours, water, 40 °C; Table 2; entries 1 and 4).

Entry	Catalyst	Phosphine (mol%)	Reaction time	Conversion (%)
1	**16** (1 mol%)	PPh_3 (1 mol%)	24 h	77
2	**16** (1 mol%)	PPh_3 (10 mol%)	24 h	0
3	**16** (1 mol%)	PPh_3 (10 mol%)	168 h	10
4	$Na[AuCl_4].2H_2O$ (1 mol%)	PPh_3 (1 mol%)	24 h	31
5	$Na[AuCl_4].2H_2O$ (1 mol%)	PPh_3 (10 mol%)	24 h	0
6	**16** (1 mol%)	dppe (1 mol%)	24 h	6
7	**16** (1 mol%)	(-)-DIOP (1 mol%)	24 h	9

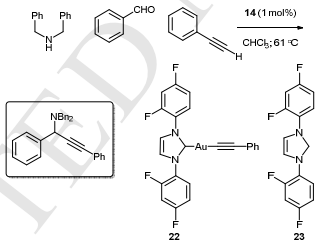
Reaction conditions: benzaldehyde (1 mmol), dibenzylamine (1 mmol), phenylacetylene (1.5 mmol), Au catalyst (mol%), H_2O, 40 °C.

Table 2: Effect of added phosphane on A^3-coupling reactions.

The $^{31}P\{^{1}H\}$ NMR spectra of the crude reaction mixtures resulting from these reactions again showed the presence of the gold(I) acetylide phosphane complex **21** ($^{31}P\{^{1}H\}$ resonance at δ 42 ppm), indicating that the gold(III) starter complexes suffer reduction during the course of the A^3-reaction. The addition of 10 mol% of triphenylphosphine completely shuts down these A^3-reactions (Table 2; entries 2 and 5) and, in these experiments at least, the $^{31}P\{1H\}$ NMR spectra of the crude reaction mixtures indicates that the reduction of the gold(III) catalyst is coupled to the oxidation of triphenylphosphine to triphenylphosphine-oxide ($^{31}P\{^{1}H\}$ resonance at δ 29 ppm).[82] Taken together, these results suggest that, under the reaction conditions employed, a common catalytic species is formed from **5**, **16**, $Na[AuCl_4]$ and **19**. We also conclude that free phosphane in the reaction medium may serve as a sink for the catalytically active species[82c] and that an active catalyst could be generated by oxidation of phosphane to phosphane oxide.

Finally, we used the fluorine tag in **14** to probe the formation of product during the course of the A^3-reactions catalysed by **14**. Again, using our standard protocol, the A^3-reaction between dibenzylamine, phenylacetylene and benzaldehyde was conducted in the presence of the fluorinated *N*-heterocyclic carbene complex **14** (1 mol%) in chloroform at reflux. The choice of solvent for this set of experiments reflects our earlier observations on solvent effects in the A^3-reaction, where it was observed that the use of chloroform has a beneficial effect on the rate of reaction.[40] In this particular example reaction proceeded to 65% conversion after 24 hours at which time an examination of the crude reaction mixture by $^{19}F\{^{1}H\}$ NMR spectroscopy indicated that all of the starter complex **14** had been consumed:[83] the resonances associated with complex **14** at δ -105.0 ppm and δ -117.9 ppm (both as doublets with $^{4}J_{FF}$=8.3 Hz) had been replaced by a set of doublets centred at δ -105.46 and -118.16 ppm ($^{4}J_{FF}$=8 Hz) and another pair of doublets at δ -104.61 and -117.62 ppm ($^{4}J_{FF}$=8.2 Hz). We have yet to characterise these new species but, given the similarity in chemistry between phosphane and NHC complexes, we speculate that these data could suggest the formation of the acetylide complex (PhCC)Au(NHC) **22** and the free carbene **23**.

A major current theme is the application of gold catalysis to asymmetric synthesis, which despite many studies remains problematic.[84a] The linear geometry of Au(I) complexes in particular enforces constraints on ligand design which thus far have limited the application of chiral Au(I) catalysts in asymmetric synthesis.[84b] Cognisant of these difficulties we wished to investigate further the total lack of enantiocontrol observed in the A^3-reactions catalysed by the starter complexes and wondered whether alternate catalytic processes, other than those discussed above could be operative in our reactions.[85]



Scheme 8: A^3-reactions catalysed by NHC Au complex **14**.

In light of reports documenting the successful use of gold nanoparticles as catalysts for A^3-coupling reactions[86-88] we wondered whether metal aggregates could be responsible for the observed catalytic activity of the *C,N* chelate complexes **4** and **16**. To this end, a standard A^3-reaction was conducted using benzaldehyde (1 mmol), dibenzylamine (1 mmol) and phenylacetylene (1.6 mmol) in $CHCl_3$ at reflux with 1 mol% of (*S*)-$[AuCl_2(\eta^2\text{-}C,N\text{-}C_6H_4CH(Me)NMe_2)]$ **4**, or $[AuCl_2(\eta^2\text{-}C,N\text{-}C_6H_4CH_2NMe_2)]$ **16** as catalyst. ^{1}H NMR spectroscopy confirmed 100% conversion to the desired A^3-coupled amine after 24 hours. The reaction mixture was then subjected to TEM analysis to test for the presence of gold nanoparticles, see Figure 6. This analysis demonstrated that nanocrystalline gold was present in the products of the reaction. The crystals were separated from the reaction mixture and characterised using transmission electron microscopy (TEM). These crystals exhibit a range of morphologies, with particles typically ranging from 5 to 50 nm in diameter. Selected area diffraction patterns show d-spacings consistent with the expected face centred cubic crystal structure of gold. High resolution imaging revealed lattice spacings consistent with gold and also showed frequent evidence of twinning, which is often observed in gold nanocrystals.[89,90] Elemental analysis using energy dispersive X-ray (EDX) spectroscopy in the TEM was used to further confirm the presence of gold in the sample. These results convincingly demonstrate that gold nanocrystals are present in the reaction mixture.

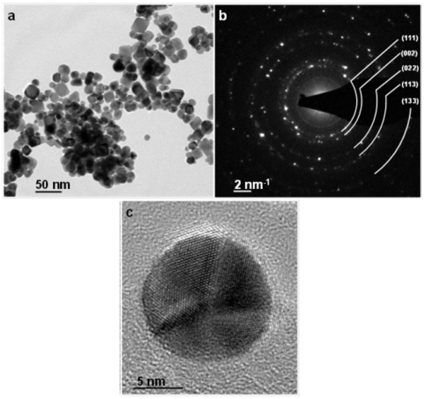
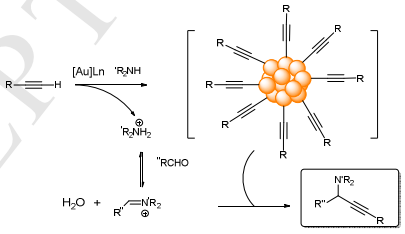


Figure 6: TEM characterisation of nanocrystals. Low magnification images show a range of particle sizes and shapes. The selected area diffraction pattern (b) shows polycrystalline rings consistent with the expected gold lattice spacings, the diffraction pattern was taken from the region shown in image a. High resolution images (c) revealing twinning in many of the particle studies.

Although the presence of gold nanoparticles does not, on its own, prove that these reactions are catalysed by gold nanoparticles it does however, in conjunction with other spectroscopic and kinetic data, suggest that gold nanoparticles may, in part, be responsible for the catalytic activity observed for the gold complexes in this study. This conclusion would also be consistent with the sluggish reactivity of gold(I) phosphine[83a] and gold(I) NHC complexes, which can be rationalised based on their increased stability, so resulting in a slower release of catalytically-active gold nanoparticles into solution.[83b] Furthermore, such a rationalisation is consistent with the lack of chiral induction observed in the coupled products when using gold complexes containing a chiral ligand. These findings may have implications for other gold NHC catalytic systems.

3. Conclusions

The synthesis of a range of new gold(I) and gold(III) complexes together with their spectroscopic characterisation and solid state structures is reported. Of these complexes [$AuCl_2(\eta^2$-*C,N*-$C_6H_4CH_2NMe_2$)] (**16**) and (*S*)-[$AuCl_2(\eta^2$-*C,N*-$C_6H_4CH(Me)NMe_2$)] **4** were found to be effective catalysts at 1 mol% levels for A^3-coupling, in water at 40 °C, giving quantitative conversion after 24 hours. A variety of substrates participated in these A^3-coupling reactions, and novel 'double-A3'-reactions could also be carried out, usually over a time course of 48 hours, to afford *bis*-propargylic amines as 1:1 mixtures of diastereoisomers. Coupling of cyclohexanone, morpholine and phenylacetylene could also be achieved using **16** and **4** (5 mol%) under neat conditions.



Scheme 9: A^3-reaction via the generation of Au-nanoparticles

Of particular significance was the lack of enantioselectivity observed in the A^3-coupling reactions promoted by the chiral complexes **4**, **5**, **11** and **12**, because obtaining enantioselectivity has previously been reported as problematic with gold, but not other metal, complexes.[84a] An initial investigation of the rate of conversion for A^3-coupling of benzaldehyde, dibenzylamine and phenylacetylene in d3-MeCN at 60 °C with 3 mol% of **16**, **19** and $Na[AuCl_4]$ as catalyst showed no significant differences. Further investigation into the nature of catalytic gold species involved the use of fluorine-tagged NHC complexes and TEM analysis of the reaction mixtures, which revealed the presence of gold nanoparticles. Taken together, the lack of chiral induction, the similar reaction profiles and the observation of gold nanoparticles lends credence to the notion that the A^3-reactions discussed in this study may in fact be promoted by gold nanoparticles,[85,91,92] as depicted in Scheme 9, that are formed from the gold complexes added as catalysts. This implies that a wide range of gold complexes might act as suitable pre-catalysts, but would have very significant ramifications for attempting to generate three-component enantioselective A^3 coupling methodology based on such gold complexes.

4. Experimental

4.1 General Considerations

All air and moisture sensitive procedures were carried out under an atmosphere of argon using standard Schlenk techniques. Diethyl ether and hexane were dried by refluxing over sodium-potassium alloy and then distilled prior to use. Tetrahydrofuran was dried by refluxing over potassium and distilled prior to use. Chemicals and compounds whose syntheses are not mentioned were obtained from commercial sources and used as received. Compounds **1**, **2**, **3**, **6**, **7**, **8**, **9**, **10**, **13** and **17** were prepared based on literature precedence, and full details are given in the ESI. NMR spectra were recorded on Bruker Avance 300, 400 or 500 MHz spectrometers. ^{1}H and ^{13}C data were referenced against the residual protio impurity or ^{13}C signals of the deuterated solvent used. ^{11}B{^{1}H}, ^{31}P{^{1}H}, ^{19}F{^{1}H} and ^{119}Sn{^{1}H} signals were referenced externally to boric acid, 85% H_3PO_4, $CFCl_3$ and $SnMe_4$ respectively. Optical rotation measurements were recorded on an Automatic Polarimeter AA-100. Elemental analyses were performed by the Microanalytical Service, The University of Manchester, Manchester, UK. Transmission electron microscopy imaging of nanocrystals was achieved by separating nanocrystals from the reaction products by centrifugation and then re-dispersion in clean chloroform. The nanocrystal suspension was drop cast onto a 300 mesh copper grid covered with a holey carbon support film and allowed to air dry. Bright field TEM images, selected area diffraction patterns and EDX spectra were acquired using a FEI Tecnai F30 microscope operating at 300 kV.

4.2 Preparation of complexes

Preparation of (*S*)-[SnClMe$_2$(η^2-*C,N*-C$_6$H$_4$CH(Me)NMe$_2$)] (3)

To dimethyltin dichloride (2.45 g, 11.15 mmol) in Et_2O (20 mL) at -78 ^{o}C was added a solution of (*S*)-2-[1-(*N,N*-dimethylamino)ethyl]phenyllithium (1.73 g, 11.15 mmol) in Et_2O (30 mL), and the mixture stirred for 1 h before warming to room temperature overnight. The solvent was removed *in vacuo* and the mixture extracted with CH_2Cl_2. The CH_2Cl_2 was removed under reduced pressure to leave an oily residue. The oil was stirred in hexane to give a white solid which was collected by filtration. Recrystallisation from MeOH gave pure (*S*)-[SnClMe$_2$(η^2-*C,N*-C$_6$H$_4$CH(Me)NMe$_2$)] **3** as a white solid (3.19 g, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.68 (s, $^{2}J_{HSn}$ = 62.17/65.18 Hz, 3H) 0.75 (s, $^{2}J_{HSn}$ = 64.43/67.06 Hz, 3H) 1.33 (d, *J* = 6.78 Hz, 3H) 2.09 (s, 3H) 2.28 (s, 3H) 3.53 - 3.68 (q, *J* = 6.78 Hz, 1H) 7.03 - 7.15 (m, 1H) 7.24 - 7.35 (m, 2H) 8.20 (dd, *J* = 5.27, 3.39 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 145.6 ($^{2}J_{CSn}$ = 38.83/40.88 Hz), 137.4 ($^{1}J_{CSn}$ = 720.53/752.99 Hz), 136.1 (J_{CSn} = 44.79 Hz), 127.8 (J_{CSn} = 13.57 Hz), 125.9 (J_{CSn} = 67.01/70.10 Hz), 123.8 (J_{CSn} = 58.09/60.91 Hz), 63.5 ($J_{CS\ n}$= 28.34 Hz), 43.2, 37.0, 13.2, 0.0 ($^{1}J_{CSn}$= 501.48/524.73 Hz), -2.0 ($^{1}J_{CSn}$= 477.41/499.58 Hz). ^{119}Sn{^{1}H} NMR (150 MHz, $CDCl_3$): δ -52.29. Calculated for $C_{12}H_{20}ClNSn$: C, 43.33; H, 6.07; N, 4.2; Found: C, 43.24; H, 5.97; N, 4.19. α_D^{24} = +25.2^{o} (c= 1, MeOH).

Preparation of (*S*)-[AuCl$_2$(η^2-*C,N*-C$_6$H$_4$CH(Me)NMe$_2$)] (4)

To (*S*)-[SnClMe$_2$(η^2-*C,N*-C$_6$H$_4$CH(Me)NMe$_2$)] (**3**) (0.17 g, 0.51 mmol) in MeCN (5 mL) was added Na[$AuCl_4$]. 2H_2O (0.2 g, 51 mmol) and the mixture refluxed for 12 h. The solvent was removed *in vacuo* to leave an oily residue which was washed with H_2O and hexane. The remaining solid was extracted into CH_2Cl_2 (5 mL) and filtered, dried over $MgSO_4$ and hexane added (7 mL). The CH_2Cl_2 was slowly removed under reduced pressure to afford (*S*)-[AuCl$_2$(η^2-*C,N*-C$_6$H$_4$CH(Me)NMe$_2$)] **4** as an off-white solid which was collected by filtration (0.18 g, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 - 7.84 (m, 1H), 7.12 - 7.43 (m, 2H), 7.07 (dd, *J* = 7.4, 1.4 Hz, 1H), 4.37 (q, ^{3}J = 6.5 Hz, 1H), 3.34 (s, 3H), 3.19 (s, 3H), 1.71 (d, ^{3}J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 148.9, 147.7, 131.4, 129.1, 128.3, 123.6, 79.3, 53.3, 48.8, 19.9. Calculated for $C_{10}H_{14}AuCl_2N$: C, 28.85; H, 3.39; N, 3.37; Found: C, 28.98; H, 3.15; N, 3.17. α_D^{24} = +82.0^{o} (c=1, CH_2Cl_2).

Preparation of (*S*)-[Au(PPh$_3$)(η^1-C$_6$H$_4$CH(Me)NMe$_2$)] (5)

To [ClAu(THT)] (0.41 g, 1.28 mmol) in Et_2O (15 mL) at -78^{o}C under argon was added (*S*)-2-[1-(*N,N*-dimethylamino)ethyl]phenyllithium (0.25 g, 1.6 mmol) in Et_2O (25 mL) and the reaction stirred for 1.5 h. PPh_3 (0.34 g, 1.29 mmol) was added and the mixture stirred for 1.5 h before warming to room temperature overnight. The Et_2O was removed under reduced pressure and the residue extracted into CH_2Cl_2 and filtered. The solvent was then removed *in vacuo* and the crude mixture stirred in hexane to give a solid which was collected by filtration. Subsequent recrystallisation of the powder with CH_2Cl_2/hexane gave pure (*S*)-[Au(PPh_3)(η^1-C$_6$H$_4$CH(Me)NMe$_2$)] (**5**) as an off-white solid (0.64 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (dd, *J*=7.8, 1.5 Hz, 3H), 7.56 (dd, *J*=7.7, 1.6 Hz, 3H), 7.32 - 7.50 (m, 11H), 7.01 - 7.14 (m, 2H), 3.83 (d, ^{3}J=6.6 Hz, 1H), 2.18 (s, 6H), 1.37 (d, ^{3}J=6.6 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 172.8 (d, J_{CP}=112.60 Hz), 153.6 (d, J_{CP}=2.77 Hz), 139.2, 134.4 (d, J_{CP}=13.84 Hz), 131.3 (d, J_{CP}=47.99 Hz), 131.1 (d, J_{CP}=1.85Hz), 129.0 (d, J_{CP}=11.08 Hz), 125.95 (d, J_{CP}=6.46 Hz), 125.8 (d, J_{CP}=5.54 Hz), 125.66.^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 44.09. Calculated for $C_{28}H_{29}AuNP$: C, 55.34; H, 4.81; N, 2.31; P, 5.10; Found: C, 55.32; H, 4.74; N, 2.24; P, 4.90. α_D^{28} = -64.5^{o} (c=1 CH_2Cl_2).

Preparation of 1,3-bis((*S*)-1'-phenylethyl) imidazolin-2-ylidene gold chloride (11)

To a stirred solution of 1,3-bis((*S*)-1'-phenylethyl)imidazolium silver chloride (**9**) (0.12 g, 0.29 mmol) in CH_2Cl_2 (15 mL) was added ClAu(THT) (0.09 g, 0.29 mmol) and the mixture stirred for 24 h. The solution was filtered through a Celite/silica plug and hexane added (10 mL). The CH_2Cl_2 was removed under reduced pressure to afford 1,3-bis((*S*)-1'-phenylethyl) imidazolin-2-ylidene gold chloride (**11**) as an off-white solid which was collected by filtration (0.13 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 - 7.43 (m, 10H, Ar-H), 6.75 (s, 2H, NCH), 6.10 (q, $^3J_{HH}$ =7.2 Hz, 2H, N-CH-Ph), 1.77 (d, $^3J_{HH}$ =7.0 Hz, 6H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 170.0, 139.3, 129.0, 128.6, 126.8, 118.2, 60.1, 20.8. Calculated for $C_{19}H_{20}AuClN_2$: C, 44.83; H, 3.96; N, 5.51; Found: C, 44.85; H, 4.05; N, 5.47. ESMS m/z: 543 (M−+Cl); HRMS calculated for $C_{19}H_{20}N_2Cl_2Au$ (M−+Cl): 543.0674, found: 543.0668. α_D^{28}= -213^o (c=1, CH_2Cl_2).

Preparation of 1,3-bis((*S*)-1'-naphthylethyl) imidazolin-2-ylidene gold chloride (12)

To a stirred solution of 1,3-bis((*S*)-1'- naphthylethyl)imidazolium silver chloride (**10**) (0.22 g, 0.42 mmol) in CH_2Cl_2 (15 mL) was added ClAu(THT) (0.135 g, 0.42 mmol) and the mixture stirred for 24 h. The solution was filtered through a Celite/silica plug and hexane added (10 mL). The CH_2Cl_2 was removed under reduced pressure to afford 1,3-bis((*S*)-1'-naphthylethyl)imidazolin-2-ylidene gold chloride (**12**) as an off-white solid which was collected by filtration (0.2 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 - 8.29 (m, 2H, Ar-H), 7.81 - 7.95 (m, 4H, Ar-H), 7.34 - 7.74 (m, 8H, Ar-H), 6.82 (q, $^3J_{HH}$ =6.8 Hz, 2H, N-CH-Ar), 6.31 (s, 2H, NCH), 1.98 (d, $^3J_{HH}$ =7.0 Hz, 6H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 170.5, 134.0, 133.4, 131.3, 130.1, 129.0, 127.4, 126.3, 124.9, 124.4, 123.2, 118.1, 56.7, 21.8. Calculated for $C_{27}H_{24}AuClN_2$: C, 53.24; H, 3.97; N, 4.60; Found: C, 53.05; H, 3.69; N, 4.64. α_D^{24}= -140^o (c=0.55, CH_2Cl_2).

Synthesis of 1,3-bis(2,4-difluorophenyl)imidazolin-2-ylidene gold(I) chloride (14)

To 1,3-bis(2,4-difluorophenyl)imidazolium chloride (**13**) (0.1 g, 0.3 mmol) in CH_2Cl_2 (10 mL) was added Ag_2O (0.045 g, 0.19 mmol) and the mixture stirred in the dark for 24 h. The suspension was filtered through celite and ClAu(THT) (0.09 g, 0.3 mmol) added. The resulting mixture was stirred for 24 h and filtered through a celite/silica plug, the solvent was removed *in vacuo*, and then CH_2Cl_2 (5 mL) added. Hexane (10 mL) was added to the solution and the CH_2Cl_2 removed under reduced pressure to afford 1,3-bis(2,4-difluorophenyl)imidazolin-2-ylidene gold(I) chloride (**14**) as a white solid which was collected by filtration (0.13 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (td, *J*=8.8, 5.5 Hz, 2H, Ar-H), 7.28 (d, *J*=1.3 Hz, 2H, NCH), 6.96 - 7.05 ppm (m, 4H, Ar-H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 172.9, 162.2 (dd, $^1J_{CF}$ = 242.72, $^3J_{CF}$ = 12.00 Hz), 155.5 (dd, ^{1}JCF = 242.72, $^3J_{CF}$ = 12.92 Hz), 128.6 (d, J_{CF} =10.15 Hz), 121.9 (m, 2C), 111.6 (dd, J_{CF} = 18.46, 4.61 Hz), 104.6 (dd, J_{CF} = 23.07, 3.69 Hz). ^{19}F{^{1}H} NMR ($CDCl_3$): δ -105.0 (d, $^4J_{FF}$= 8.3 Hz), -117.9 (d, $^4J_{FF}$= 8.3 Hz). Calculated for: $C_{15}H_8AuClF_4N_2$: C, 34.32; H, 1.54; N, 5.34; Found: C, 34.51; H, 1.84; N, 5.25. ESMS m/z: 559 (M−+Cl); HRMS calculated for $C_{15}H_8N_2Cl_2F_4Au$ (M−+Cl): 558.9671, found: 558.9655.

Preparation of [$AuCl_2(\eta^2$-*C,N*-$C_6H_4CH_2NMe_2$)] (16)

To a solution of Na[$AuCl_4$]. $2H_2O$ (0.2 g, 0.5 mmol) in H_2O (25 mL) was added (2-$(Me_2NCH_2)C_6H_4BO)_3$ (0.08 g, 0.17 mmol) in MeCN (5 mL) and the yellow mixture refluxed for 48 h. The acetonitrile was removed under reduced pressure, the mixture filtered and the solid extracted into CH_2Cl_2 (15 mL) and hexane added (10 mL). The CH_2Cl_2 was removed slowly under reduced pressure to induce crystallization of [$AuCl_2(\eta^2$-*C,N*-$C_6H_4CH_2NMe_2$)] **16** which was collected by filtration as an off-white solid (0.1 g, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J*=7.6 Hz, 1H, Ph-H), 7.15 - 7.31 (m, 2H, Ph-H), 7.04 - 7.14 (m, 1H, Ph-H), 4.34 (s, 2H, CH), 3.26 (s, 6H, NMe_2). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 148.0 (Ph-C), 143.6 (Ph-C), 131.3 (Ph-C), 129.1 (Ph-C), 128.1 (Ph-C), 123.2 (Ph-C), 75.9 (CH_2), 53.8 (NMe_2). Calculated for $C_9H_{12}NAuCl_2$: C, 26.9; H, 3.0; N, 3.5; Found: C, 26.9; H, 2.7; N, 3.2.

Preparation of 1,3-bis((*S*)-1'-naphthylethyl) imidazolin-2-ylidene gold bis(trifluoromethanesulfonyl)imide (17)

To a stirred solution of 1,3-bis((*S*)-1'-naphthylethyl) imidazolin-2-ylidene gold chloride (**12**) (0.1 g, 0.16 mmol) in CH_2Cl_2 (15 mL) was added $AgNTf_2$ (0.06 g, 0.16 mmol) and the mixture stirred for 15 mins. The solution was filtered through Celite and hexane added (10 mL). The CH_2Cl_2 was removed under reduced pressure to afford 1,3-bis((*S*)-1'-naphthylethyl) imidazolin-2-ylidene gold bis(trifluoromethanesulfonyl)imide (**17**) as an off-white solid which was collected by filtration (0.1 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 - 8.22 (m, 2H, Ar-H), 7.72 - 8.01 (m, 4H, Ar-H), 7.47 - 7.68 (m, 8H, Ar-H), 6.70 (q, $^3J_{HH}$=6.8 Hz, 2H, N-CH-Ar), 6.58 (s, 2H, NCH), 2.01 (d, $^3J_{HH}$=7.0 Hz, 6H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 163.0, 134.0, 133.4, 131.1, 130.2, 129.1, 127.5, 126.4, 125.0, 124.2, 122.8, 119.4 (q, $^1J_{CF}$=323.02 Hz), 118.9, 57.2, 21.8. ^{19}F{^{1}H} NMR ($CDCl_3$): δ -75.37. ESMS m/z: 280 (M− NTf_2) 614 (M^+ NHCAu + MeCN).

4.3 A^3-coupling procedures

Entry 1: To a dry nitrogen flushed Schlenk flask was added benzaldehyde (100 µL, 1 mmol) piperidine (116 µL, 1.1 mmol), phenylacetylene (162 µL, 1.5 mmol), H_2O (2 mL) and (*S*)-[$AuCl_2(\eta^2$-C,N-$C_6H_4CH(Me)NMe_2$)] **4** (4 mg, 1 mol %). The mixture was stirred at 40°C for 24 h, then extracted with CH_2Cl_2, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by column chromatography on silica gel using hexane/EtOAC eluent.

Full details of all A^3-coupling reactions are given in the ESI.

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Supplementary Data.

Supplementary data, detailing the preparation and spectroscopic data, of compounds discussed in this article can be found at http://dx.doi.org/10.1016/j.jorganchem

Copies of cif files have been deposited with the CCDC, Cambridge. CCDC 889456 (**4**), 889457 (**5**), 943937 (**9**), 943938 (**11**), 943935 (**12**) and 943936 (**14**) contain the supplementary crystallographic data for this paper. These files can be obtained, free of charge, from the CCDC *via* www.ccdc.cam.ac.uk/data_request/cif. Complex **9** was also subjected to a single crystal X-ray diffraction study, see ESI for ORTEP and collection details.

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