COMMUNICATION

Bis-cyclometallated Gold(III) Complexes as Efficient Catalysts for Synthesis of Propargylamines and Alkylated Indoles

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Stable bis-cyclometallated gold(III) complexes were developed as efficient catalysts for organic transformation reactions by using two strategies: (1) construction of distorted square planar gold(III) complexes and (2) dual catalysis by gold(III)
10 **complexes and silver salts.**

Gold catalysis has attracted significant attention in catalysis research due to its superior reactivity, excellent selectivity and high functional group tolerance.[1] Studies on the use of simple gold salts (e.g. AuCl and AuCl$_3$) as catalysts for organic synthesis
15 have been considerably reported.[2] However, the instability of simple gold salts in catalytic cycles leading to low product turnovers is an unresolved issue.[3] In this connection, gold(I) complexes have been largely developed as efficient catalysts to achieve novel synthetic transformations.[1,4] However, the
20 development of gold(III) complexes for catalysis remains largely unexplored.

Gold(III) complexes have a square planar geometry with four coordination sites, and in principle the reactivity of the gold(III) reaction centre can be easily fine-tuned by diverse ligand design
25 in a modular approach.[5] However, a significant challenge in the development of gold(III) complexes as efficient catalysts is to strike a balance between stability and reactivity. In general, the stability of gold(III) ions significantly increases upon complexation with ligands. However, stable gold(III) complexes
30 generally exhibit poor catalytic activity. We envision that novel ligand design and substrate activation strategies are of importance in the pursuit of gold(III) catalysis for organic synthesis.

Over the years, we have been developing gold catalysis for organic transformation reactions.[6] In particular, we are interested
35 to employ cyclometallated gold(III) complexes[7] as catalysts for organic synthesis.[8] Recently, we found that stable bis-cyclometallated gold(III) catalysts are able to exhibit high catalytic activity in organic synthesis through two novel strategies: (1) formation of coordinatively saturated distorted square planar
40 gold(III) complexes using bulky C,N donor ligands and (2) gold-silver dual catalysis for substrate activation.
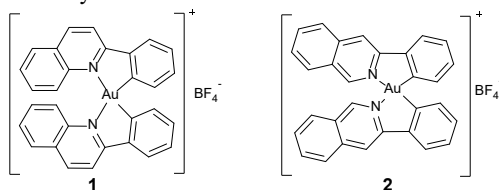

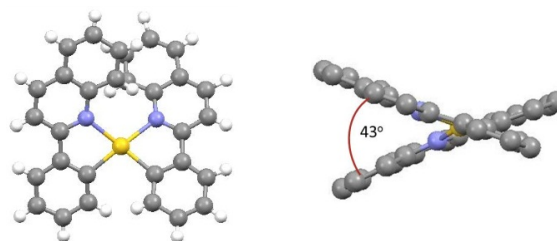**Fig. 1** Bis-cyclometallated gold(III) complexes **1** and **2**.

45 **Fig. 2** Crystal structure of **1** in top view (left) and side view (right). Anion was omitted for clarity.

Bis-cyclometallated gold(III) complexes [Au(C^N)$_2$][BF$_4$] **1** (HC^N = 2-phenylquinoline) and **2** (HC^N = 3-phenylisoquinoline) were synthesized by transmetallation of
50 KAuCl$_4$ with their corresponding organomercury complexes in 75% and 42% yields, respectively (Fig. 1). Notably, a distorted square planar geometry[9] of **1** was revealed by X-ray crystallography (Fig. 2). The two 2-phenylquinoline ligands in **1** were tilted to give a dihedral angle of 43°. The Au-N bond length
55 is elongated (up to 0.141 Å) when compared with literature-known square planar cyclometallated gold(III) complexes[10] (Table S2, ESI†). Probably due to the steric repulsion between the quinoline rings, the Au-N bond length is elongated and a non-planar geometry is adopted in order to maintain coordination of
60 ligands to the gold(III) centre. On the basis of NMR spectroscopy and literatures, a typical square planar geometry is expected for complex **2**. The gold(III) complexes **1** and **2** were characterized by ^{1}H NMR, ^{13}C NMR, and ESI-MS, and were found to be air- and water-stable.
65 Studies on the catalytic activities of **1** and **2** in the three-component coupling reaction of aldehydes, amines and alkynes for propargylamine synthesis[11] are depicted in Table 1. Using 1 mol % of complex **1** with a distorted square planar geometry, propargylamine **6a** was obtained in 83% isolated yield at 40 °C in
70 24 h under air (entry 1). As shown in entry 2, 60% isolated yield of **6a** was obtained even with 0.1 mol % of **1**, which was found to be comparable with our previous works.[6a,8a,8c] Note that complex **1** (1 mol %) was able to catalyze the reaction at room temperature (entry 3). In contrast, complex **2** exhibited poor catalytic activity.
75 Using 1 mol % of **2** only gave 8% isolated yield (entry 4) while no reaction was observed with 0.1 mol % of **2** (entry 5).

The significantly higher catalytic activity of **1** than that of **2** could be attributed to their difference in geometry. Complex **1** is of a distorted square planar geometry with elongated bond

lengths. Hence, ligand dissociation of **1** to generate a highly reactive gold(III) reaction centre for alkyne activation would be more favorable than complex **2**. It is envisioned that such design of distorted gold(III) complexes would be applicable in catalyzing other classes of organic reactions.

Table 1 Bis-cyclometallated gold(III) complex-catalyzed three-component coupling reaction for propargylamine synthesis.[a]

Entry	Catalyst (mol %)	Isolated Yield (%)
1	**1** (1)	83
2	**1** (0.1)	60
3[b]	**1** (1)	25
4	**2** (5)	8
5	**2** (1)	0

[a] Reaction conditions: **3a** (0.5 mmol), **4a** (0.55 mmol) and **5a** (0.75 mmol) in H$_2$O (1 mL). [b] room temperature.

Next, complex **1** was used in stereoselective synthesis of propargylamines **6b–6h** with 70–90% isolated yields and diastereomeric ratio (*dr*) up to > 99:1 (Fig. 3). In addition, complex **1** was able to promote selective modification of D-raffinose aldehyde with 85% aldehyde conversion.[8b]

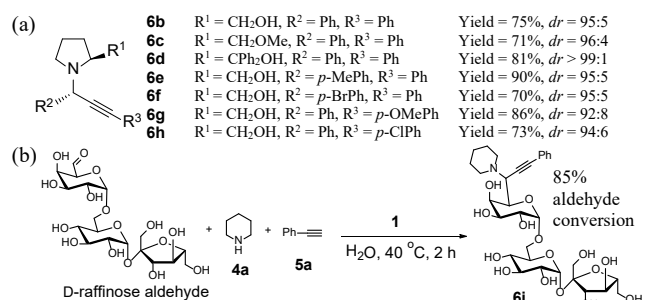|		
6b	R^1 = CH$_2$OH, R^2 = Ph, R^3 = Ph	Yield = 75%, *dr* = 95:5
6c	R^1 = CH$_2$OMe, R^2 = Ph, R^3 = Ph	Yield = 71%, *dr* = 96:4
6d	R^1 = CPh$_2$OH, R^2 = Ph, R^3 = Ph	Yield = 81%, *dr* > 99:1
6e	R^1 = CH$_2$OH, R^2 = *p*-MePh, R^3 = Ph	Yield = 90%, *dr* = 95:5
6f	R^1 = CH$_2$OH, R^2 = *p*-BrPh, R^3 = Ph	Yield = 70%, *dr* = 95:5
6g	R^1 = CH$_2$OH, R^2 = Ph, R^3 = *p*-OMePh	Yield = 86%, *dr* = 92:8
6h	R^1 = CH$_2$OH, R^2 = Ph, R^3 = *p*-ClPh	Yield = 73%, *dr* = 94:6

Fig. 3 (a) Substrate scope of propargylamine synthesis catalyzed by **1**. (b) Modification of D-raffinose aldehyde via three-component coupling reaction.

In the next section, a gold-silver cooperative dual catalysis strategy[12] was used in bis-cyclometallated gold(III) complex-catalyzed indole alkylation[13] (Table 2). According to the proposed reaction mechanism,[14] alkylated indole **9a** was formed by metal-catalyzed cyclization of alkynyl alcohol **7a** to generate enol ether *in situ* followed by C–H addition of indole **8a** to the enol ether. Through systematic screening, we found that silver salts are able to work synergistically with bis-cyclometallated gold(III) complexes in the indole alkylation.

Using **1** (2.5 mol %) with AgBF$_4$ (5 mol %), alkynyl alcohol **7a** reacted with indole **8a** to give alkylated indole **9a** in 80% isolated yield at room temperature in 2 h (entry 1). The reaction using complex **2** (2.5 mol %) with AgBF$_4$ (5 mol %) gave 47% isolated yield (entry 2). Combination of **1** with Zn(OTf)$_2$ or Yb(OTf)$_3$ could also catalyze the reaction to afford 76% and 39% isolated yields, respectively (entries 3–4). In the control experiments (entries 5–9), poor yields (10–13%) or no product formation were found when only single metal catalyst was used. Catalyst screening using various metal salts was also conducted (see ESI†). These findings indicate that proper combination of dual metal catalysts[15] is a feasible approach to render stable bis-

cyclometallated gold(III) complexes as efficient catalysts in organic transformation reactions.

Table 2 Screening of catalysts for synthesis of alkylated indoles.[a]

Entry	Catalyst (mol %)	Isolated Yield (%)[b]
1	**1** (2.5) + AgBF$_4$ (5)	80
2	**2** (2.5) + AgBF$_4$ (5)	47
3	**1** (2.5) + Zn(OTf)$_2$ (5)	76
4	**1** (2.5) + Yb(OTf)$_3$ (5)	39
5	**1** (5)	13[c]
6	**2** (5)	0
7	AgBF$_4$ (5)	10[c]
8	Zn(OTf)$_3$ (5)	0
9	Yb(OTf)$_3$ (5)	0

[a] Reaction conditions: **7a** (0.24 mmol) and **8a** (0.2 mmol) in CH$_2$Cl$_2$ (2 mL). [b] Isolated yield. [c] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

The substrate scope of the dual metal catalysis for indole alkylation was demonstrated by using alkynyl alcohols of different chain lengths **7a–7g** and indoles with different substituents **8a–8j** to afford alkylated indoles **9a–9p** with up to 94% isolated yields (Table 3). The reactivity and regioselectivity of the present reaction were found to be consistent with literature reports.[14,16]

Table 3 Gold(III) complex-silver catalyzed cyclization-addition reactions of alkynyl alcohols **7a–7g** and substituted indoles **8a–8i**.[a]

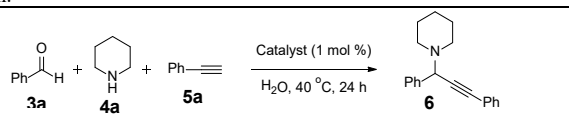| Entry	n	R^1	R^2	R^3	X	Product	Isolated Yield (%)
1	1	CH$_3$	CH$_3$	H	H	**9a**	80
2	1	C$_2$H$_5$	CH$_3$	H	H	**9b**	74
3	1	C$_3$H$_7$	CH$_3$	H	H	**9c**	78
4	1	Ph	CH$_3$	H	H	**9d**	75
5	2	Ph	CH$_3$	H	H	**9e**	74[b]
6	3	C$_4$H$_9$	CH$_3$	H	H	**9f**	84[c]
7	3	H	CH$_3$	H	H	**9g**	94[c]
8	1	CH$_3$	CH$_3$	H	Br	**9h**	80
9	1	CH$_3$	CH$_3$	H	OMe	**9i**	80
10	1	CH$_3$	CH$_3$	H	NO$_2$	**9j**	67[d]
11	1	CH$_3$	CH$_3$	CH$_3$	H	**9k**	40
12	1	CH$_3$	H	H	H	**9l**	75
13	1	CH$_3$	H	H	Br	**9m**	71[e]
14	1	CH$_3$	H	H	OMe	**9n**	53
15	1	CH$_3$	H	H	NO$_2$	**9o**	70[d]
16	1	CH$_3$	H	CH$_3$	H	**9p**	58

[a] Reaction conditions: **7a–7g** (0.24 mmol) and **8a–8g** (0.2 mmol) in CH$_2$Cl$_2$ (2 mL). [b] 5-exo-dig cyclized product was formed. [c] 6-exo-dig cyclized products were formed. [d] 16 h. [e] 4 h.

An important advantage of using gold(III) complexes over simple gold(III) salts is the recyclability in catalysis. The recyclability experiments of catalyst **1** in propargylamine synthesis were conducted (Table 4). Catalyst **1** could be repeatedly used for 7 cycles leading to 638 product turnovers in

total. However, the conversion of using $KAuCl_4$ decreased significantly leading to only 29% conversion in the 7th cycle. These findings clearly indicate the recyclability of catalyst **1**.

Next, we set out to examine the recyclability of catalyst **1** in the dual catalysis of indole alkylation (Table 5). Catalyst **1** could be repeatedly used for 11 cycles to give 73–88% conversions with addition of $AgBF_4$ at the 6th and 11th cycles. At the end of the 10th cycle, complex **1** was found to remain intact by ESI-MS analysis of the reaction mixture. These results suggest that catalyst **1** is stable under the reaction conditions and could be reused with further addition of $AgBF_4$. Yet, the recyclability experiments conducted using $KAuCl_4$ or "$KAuCl_4 + AgBF_4$" as catalysts gave no product formation in the 2nd cycle.

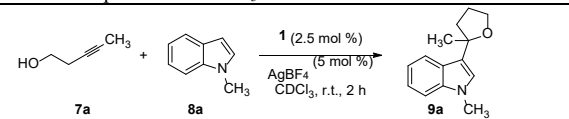**Table 4** Recyclability experiments of **1** and $KAuCl_4$ in three-component reaction.[a]

Cycle	1	2	3	4	5	6	7
Conversion (%)[b] by **1**	99	97	93	85	89	86	89
Conversion (%)[b] by $KAuCl_4$	99	94	82	65	51	38	29

[a] Reaction conditions: **3a** (1 mmol), **4a** (1.1 mmol) and **5a** (1.5 mmol) in H_2O (1 mL). [b] Determined by ^1H NMR.

Table 5 Recyclability experiment of "**1** + $AgBF_4$" in the reaction of **7a** and **8a** at room temperature in $CDCl_3$.[a]

Cycle	1	2	3	4	5	6[c]	7	8	9	10	11[c]
Conversion (%)[b]	85	81	81	78	73	88	87	85	81	74	83

[a] Reaction conditions: **7a** (0.24 mmol) and **8a** (0.2 mmol) in $CDCl_3$ (2 mL). [b] Determined by ^1H NMR. [c] Additional $AgBF_4$ (5 mol %) was added.

In conclusion, we have developed two novel strategies rendering stable bis-cyclometallated gold(III) complexes as efficient catalysts in organic synthesis by (1) ligand design and (2) dual catalysis.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental details, NMR spectra of new compounds, and crystallographic data of complex **1** (CCDC 946727). See DOI: 10.1039/b000000x/

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