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Triazole−Au(I) Complexes: A New Class of Catalysts with Improved Thermal Stability and Reactivity for Intermolecular Alkyne Hydroamination

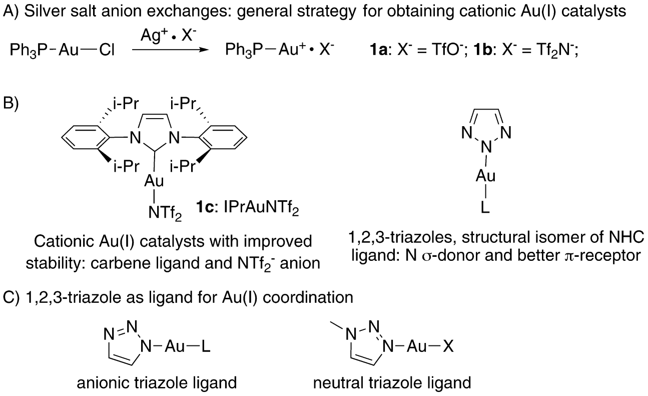
Haifeng Duan, Sujata Sengupta, Jeffrey L. Petersen, Novruz G. Akhmedov, and Xiaodong Shi*

C. Eugene Bennett Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506

Received May 20, 2009; E-mail: Xiaodong.Shi@mail.wvu.edu

The recent success of homogeneous gold catalysis is clearly demonstrated by the large number of reports in the literature[1] and a significant portion of the new research activity has been contributed by cationic Au(I) complexes.[2] Despite their remarkable reactivity toward the electrophilic activation of alkynes, one challenge for simple cationic Au(I) complexes, such as the popular $PPh_3Au^+\cdot OTf^-$ (**1a**), is overcoming their poor stability at high temperature (leading to formation of a gold mirror and gold nanoparticles).[3] However, in order to activate some less reactive substrates, such as internal alkynes, harsher reaction conditions are usually required.[4] Therefore, new Au(I) catalysts that may overcome the *reactivity−stability dilemma* are highly desirable and would thereby open new temperature ranges for this rapidly growing research field.

Scheme 1



Among the reported systems, N-heterocyclic carbenes (NHCs) have been suggested as a good ligand choice, giving improved catalyst stability at higher temperatures by the formation of metal−ligand back-bonding (Scheme 1B).[5] In addition, nitrogen counteranions such as Tf_2N^- have also been found to help the catalyst stability without significantly decreasing the reactivity by forming dynamic Au−N coordination.[6] Our group has recently developed new synthetic methods for substituted 1,2,3-NH-triazole derivatives[7] and applied the NH-triazoles as ligands in transition-metal coordination.[8] Preliminary studies have also shown that triazole−Rh(I) complexes provide much better stability while retaining good catalytic reactivity. In comparison with the more expensive NHC ligands, simple triazole compounds possess nitrogen σ-donor and lower LUMO aromatic antibonding orbitals for potentially improved metal back-bonding. Therefore, we envisioned that triazoles may be applied as ligands to produce new cationic Au catalysts with improved stability and effective reactivity, especially at high temperatures (Scheme 1C).[9] Herein, we report thermally stable triazole−Au catalysts for intermolecular hydroamination of unprotected amines with both terminal and internal alkynes that give excellent yields (>90%) and high efficiency (0.1% catalyst loading) at high temperature (80 °C).

The triazole−Au complexes **2a** ($PPh_3Au\cdot Btz$) and **2b** ($PPh_3Au\cdot PTz$) were prepared in quantitative yields using a preparation procedure similar to the one reported recently for triazole−Rh complexes.[8] The structures of **2a** and **2b** were determined by X-ray diffraction [see the Supporting Information (SI)], which revealed N1 coordination in **2a** and N2 coordination in **2b**. Neutral triazole-bound Au(I) complexes were also successfully prepared by treating the corresponding triazole and PPh_3AuCl mixtures with AgOTf (Scheme 1A). Removal of the AgCl precipitate gave clear solutions, which were then concentrated to afford complexes **3a−c** ($PPh_3Au\cdot BtzH$, $PPh_3Au\cdot BtzMe$, and $PPh_3Au\cdot BtzBn$, respectively) in near-quantitative yields. All of these triazole−Au complexes are white solids that are stable with respect to air and moisture, including the cationic gold complexes **3a−c**. Moreover, complex **3a** could also be prepared directly by the treatment of **2a** with HOTf. It is important to notice here that the X-ray structure of **3a** revealed coordination between the neutral triazole and the Au cation in the presence of a TfO^- literal ion as the counteranion. This result provides strong evidence for the proposed neutral triazole−Au coordination in the presence of other counteranions.

Because the same PPh_3 ligand was used in all these complexes, ^{31}P NMR became one good indicator in monitoring the electronic effect of different ligands on the Au cation, which may directly relate to its catalytic reactivity. A comparison of the ^{31}P chemical shifts of different Au complexes is shown in Figure 1. The literal ion complex $PPh_3Au^+\cdot OTf^-$ **1a** (highly reactive) gave a ^{31}P chemical shift of 28.80 ppm, while the covalently linked complex PPh_3Au-Cl (stable but less reactive) showed a ^{31}P NMR chemical shift further downfield at 34.31 ppm.

As suggested in the literature, the Tf_2N anion forms dynamic coordination with the Au cation, thereby improving the thermal stability of the catalyst.[6] This was supported by the ^{31}P NMR data, where **1b** gave a chemical shift of 31.60 ppm, which is located between those for the Au^+ literal ion and the strongly covalent complex PPh_3AuCl. We were subsequently pleased to observe a similar electronic influence in our triazole-bound Au complexes. Thus, the complexes **2b** and **3d** (possessing similar binding affinities at the N1 and N2 positions) were then investigated by variable-temperature (VT) NMR studies (note: different ^{31}P signals appear for various N isomers).

As shown in Figure 2A, dissolving pure N2 isomer **2b** gave two broad signals at room temperature, indicating the fast exchange between the N2 and N1 isomers in solution. The N3 isomer was not observed because of C4-phenyl steric hindrance. The exchange rate was decreased at low temperature, resulting in two sharp signals. Signal line shape analysis (based on VT NMR data from −55 to 60 °C) gave a good linear correlation ($r^2 = 0.99$; see details in the SI), affording $E_a = 5.9 \pm 0.4$ kcal mol^{-1}, $\Delta H^\ddagger = 5.4 \pm 0.4$ kcal mol^{-1}, and $\Delta S^\ddagger = -30.9 \pm 1.4$ cal mol^{-1} K^{-1}. In comparison,

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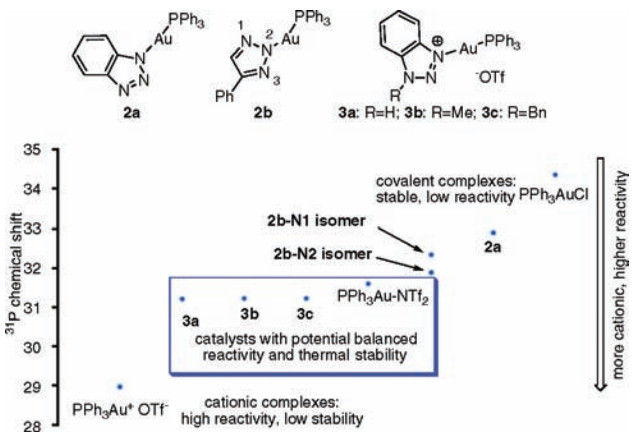


Figure 1. ^{31}P NMR chemical shifts of the different Au(I) complexes at 28 °C. Structures of **2a**, **2b**, and **3a** were determined by X-ray crystallography and are shown in the SI along with ^{31}P NMR comparisons at −55 and 60 °C. Complex **2b** gave two signals in solution, corresponding to the two different N isomers that were equilibrated in solution.

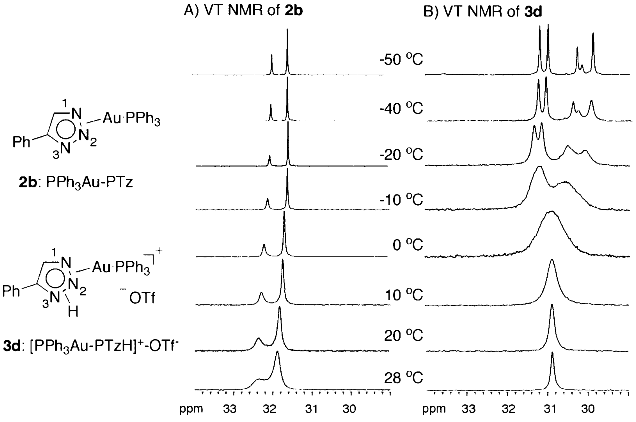


Figure 2. VT NMR spectra of (A) **2b** and (B) **3d**, showing dynamic exchange of triazole−Au binding with different kinetics.

dissolving cationic complex **3d** in solution gave one sharp signal at room temperature (Figure 2B). With both H and Au coordinated on the triazole, six regioisomers could theoretically be produced (i.e., N3-H/N1-Au, N3-H/N2-Au, etc.). As a result, multiple ^{31}P signals were obtained at lower temperatures. Because of the great complexity in **3d**, line shape analysis could not be applied. However, it was clear that faster exchange was associated with neutral triazole ligands, where a lower temperature was needed in order to obtain separated ^{31}P signals under the same conditions. Notably, the benzotriazole Au complexes gave dominant N1 binding between −55 and 60 °C, which made them unsuitable for this VT NMR study. However, considering the similar functional group, it is expected that complexes **2a** and **3a−c** would possess the same dynamic coordination nature, which is crucial for the catalytic reactivity and potential Au cation stability. To further test our hypothesis that this dynamic triazole−Au coordination may help the thermal stability of the Au catalyst, especially at high temperature, the hydroamination of internal alkyne **4a** with aniline (**5a**) was investigated with the presence of different Au(I) catalysts.

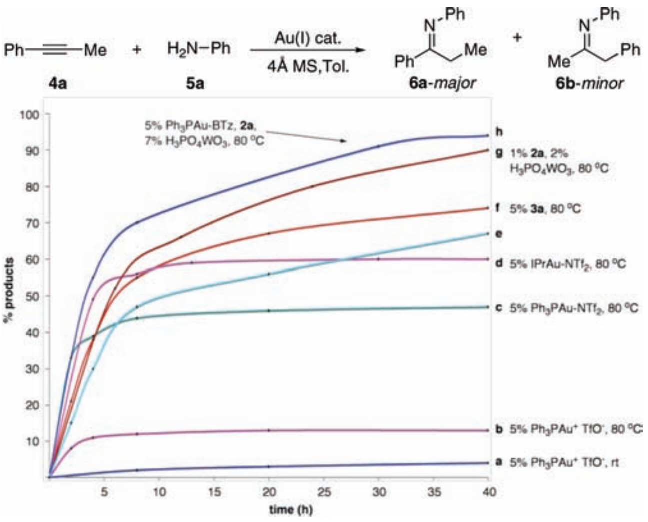


Figure 3. Reaction process profile: (a) 5% **1a**, rt; (b) 5% **1a**, 80 °C; (c) 5% **1b**, 80 °C; (d) 5% **1c**, 80 °C; (e) 5% **3a** + 5% benzotriazole, 80 °C; (f) 5% **3a**, 80 °C; (g) 1% **2a**, 2% $H_3PO_4 \cdot 12WO_3$, 80 °C; (h) 5% **2a**, 7% $H_3PO_4 \cdot 12WO_3$, 80 °C.

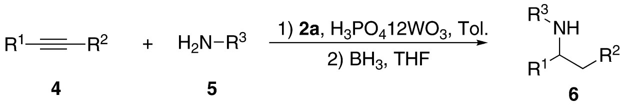
Table 1. Comparison of Au(I) Catalysts in Internal Alkyne Hydroamination[a]

	Au(I) cat	loading	cocatalyst	temp (°C)	**6a/6b**[b]	yield (%)[c]
1	**1a**	5%	−	r.t.	n.d.	4
2	**1a**	5%	−	80	4:1	13
3	**1b**	5%	−	80	4:1	47
4	**1c**	5%	−	80	1.2:1	60
5	**3a**	5%	−	80	6:1	74[d]
6	**3d**	5%	−	80	3:1	58[d]
7	**3a**	5%	BtzH (5%)	80	6:1	67
8	**2a**	5%	$H_3PO_4 \cdot 12WO_3$ (5%)	80	6:1	94[d]
9	**2a**	5%	$H_3PO_4 \cdot 12WO_3$ (5%)	100	1.5:1	92[d]
10	**2a**	**1%**	$\mathbf{H_3PO_4 \cdot 12WO_3}$ **(2%)**	**80**	**6:1**	**91**[d]
11	**2b**	**1%**	$\mathbf{H_3PO_4 \cdot 12WO_3}$ **(2%)**	**80**	**6:1**	**86**[d]
12	**1c**	5%	$H_3PO_4 \cdot 12WO_3$ (5%)	80	1.2:1	45
13	−	−	$H_3PO_4 \cdot 12WO_3$ (10%)	80	n.d.	n.r.
14	−	−	TfOH (10%)	80	n.d.	n.r.

[a] General reaction conditions: **4a** (1.0 equiv), **5a** (1.2 equiv), and catalysts were mixed in dry toluene ([**4a**] = 0.3 M). The reactions were monitored by TLC. [b] Determined by NMR analysis of the crude reaction mixture. [c] NMR yield using 1,3,5-trimethoxybenzene as an internal standard. [d] Isolated yield of reduced amine after treating **6a/6b** with BH_3 in THF.

As indicated by the reaction profiles (Figure 3), in order to achieve effective internal alkyne hydroamination, higher temperature is needed (Figure 3a,b). All of the tested *nontriazole* Au catalysts clearly suffered from thermal decomposition over time, even IPrAu·NTf_2 (**1c**) (Figure 3d). Anionic triazole-ligand-bound Au complex **2a** did not promote the reaction because of a lack of reactivity. However, with the application of neutral triazole-bound Au complex **3a**, significant improvement was obtained, giving the desired products in good yields (Figure 3f). This ligand effect was further supported by the addition of excess triazole ligand (Figure 3e), where a lower reaction rate was observed, suggesting the coordination of the triazole ligand with the Au cation (competition with the alkyne substrate). The reaction was further improved with the addition of $H_3PO_4 \cdot 12WO_3$,[10] *where an excellent yield (91%) was achieved even with only 1% catalyst loading.* Notably, the addition of $H_3PO_4 \cdot 12WO_3$ with **1c** did not improve the reaction performance (Table 1, entry 12), eliminating the possibility of an acid effect in this improved thermal stability of the triazole−Au catalyst. Application of 4-phenyltriazole complexes (**2b** and **3d**) gave reactivity similar to that of the benzotriazole complexes (entries 5−6 and 10−11), suggesting that the dynamic coordination with Au cation is a general property for 1,2,3-triazoles. To the best of our knowledge, these triazole−Au complexes are by far the most efficient Au catalysts in promoting internal alkyne activation. Applications of the new catalyst **2a** with different alkynes and

Table 2. Reaction Substrate Scope[a]



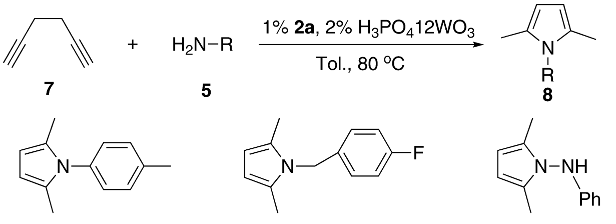
Alkyne	Amine (R^3)	**2a** (%)	yield (%)[b]	Alkyne	Amine (R^3)	**2a** (%)	**a:b**[d]	yield (%)[b]
Ph-C≡C-H **4b**	Ph	**0.1**	**6c**: 94	Ph-C≡C-Me **4a**	Ph	**1.0**	6:1	**6a/6b**: 91
	p-Me-Ph	**0.1**	**6d**: 92		p-Me-Ph	**1.0**	6:1	**6r**: 89
	p-OMe-Ph	**0.1**	**6e**: 93		p-OMe-Ph	**1.0**	5:1	**6s**: 86
	o-Cl-Ph	**0.1**	**6f**: 94		p-F-Ph	**1.0**	6:1	**6t**: 93
	p-F-Ph	**0.1**	**6g**: 97	Ph-C≡C-Et **4g**	Ph	**1.0**	3:1	**6u**: 91
	NHPh	**0.1**	**6h**: 98	Ph-C≡C-Bu **4h**	p-F-Ph	**1.0**	3:1	**6v**: 90
	2,4,6-tri-Me-Ph	**0.1**	**6i**: 96	Pr-C≡C-Me **4i**	p-Me-Ph	**1.0**	2:1	**6w**: 85
Cy-C≡C-H **4c**	Ph	**0.1**	**6j**: 87	Ph-C≡C-H **4b**	Ts	3.0	-	**6x**: 95
	p-F-Ph	**0.1**	**6k**: 90		p-fluoro-Bn	10	-	**6y**: 44
Bu-C≡C-H **4d**	Ph	**0.1**	**6l**: 81					
	p-F-Ph	**0.1**	**6m**: 86		morpholine	10	-	**6z**: 70
Ph-C≡C-Ph **4e**	Ph	**1.0**	**6n**: 83					
	p-Me-Ph	**1.0**	**6o**: 84		cbz	10	-	**6aa**: 30
Pr-C≡C-Pr **4f**	p-Me-Ph	**1.0**	**6p**: 86					
	o-Cl-Ph	**1.0**	**6q**: 83		PhCO	10	-	**6ab**: 11

[a] General reaction conditions: **4a** (1.0 equiv), **5a** (1.2 equiv), and catalysts were mixed in dry toluene ([**4a**] = 0.3 M). The reactions were monitored by TLC. [b] NMR yield using 1,3,5-trimethoxybenzene as an internal standard. [c] Isolated yield of reduced amine after treating **6a/6b** with BH_3 in THF. [d] Determined by NMR analysis.[11]

amines were then performed. The reaction substrate scope is shown in Table 2.

As expected, the triazole−Au catalyst gave a wide reaction substrate scope. For more reactive terminal alkynes, excellent yields (generally >90%) were achieved with only 0.1% catalyst loading. With less reactive internal alkynes, higher catalytic loading was needed; 1% loading generally produced the desired hydroamination products in >85% yield. Moreover, with increased catalyst loading (10%), the extremely challenging intermolecular, unprotected aliphatic amine hydroaminations to afford **6y** and **6z** were achieved, though with modest yields. Since the key side reaction for aliphatic amine hydroamination is the decomposition of the imine, the diyne **7** was applied to trap the active imine intermediate through a second intramolecular hydroamination.[12] The substituted pyrroles **8** were prepared in excellent yields, as shown in Scheme 2.

Scheme 2



8a: 1% Au cat., 2% acid, 90% yield

8b: 5% Au cat., 7% acid, 89% yield

8c: 1% Au cat., 2% acid, 97% yield

In conclusion, the investigation of triazole−Au coordination by variable-temperature NMR spectroscopy revealed a dynamic coordination between the triazole and the Au(I) cation, leading to the discovery of a new class of thermally stable cationic Au(I) catalysts. The superior stability and cationic Au reactivity of these catalysts were evidenced in challenging transformations, such as intermolecular internal alkyne hydroamination and reactions with unprotected aliphatic amines. It is our belief that this catalytic system may *open a new temperature range* for homogeneous Au(I) catalysis, and therefore, the discovery of new reactivities is expected in the near future.

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Supporting Information Available: Detailed experimental procedures, spectral data for all new compounds, and CIF files for compounds **2a**, **2b**, and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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