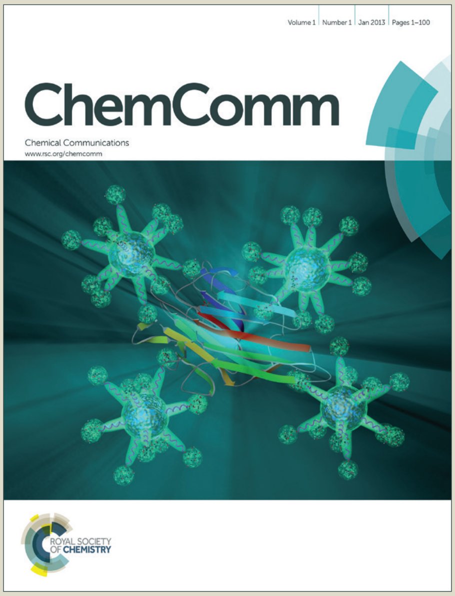
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name

COMMUNICATION

Gold-catalyzed selective oxidation of 4-Oxahepta-1,6-diynes to 2*H*-pyran-3(6*H*)-ones and chromen-3(4*H*)-ones via the *β*-gold vinyl cation intermediates

Received 00th January 20xx,
Accepted 00th January 20xx

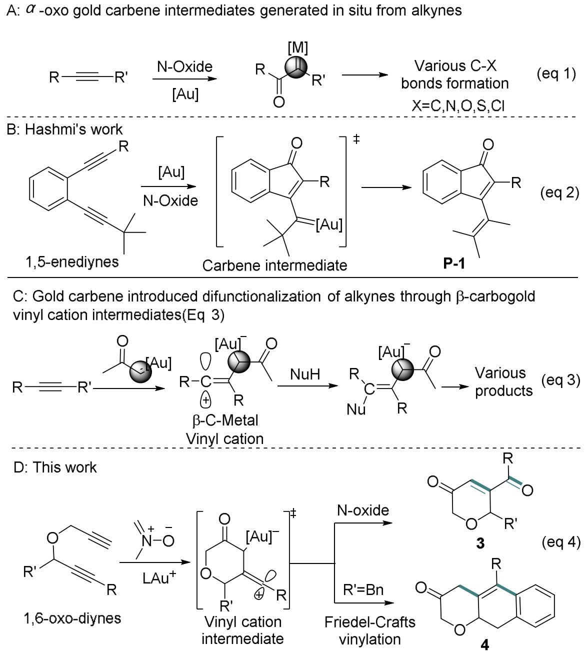
DOI: 10.1039/x0xx00000x

www.rsc.org/

Kegong Ji,* Xiang Liu, Bowen Du, Fang Yang, Jinming Gao

The α-oxo gold carbenes generated in situ via gold-catalyzed selective oxidation of 4-oxahepta-1,6-diynes were effectively trapped by internal alkynes, resulting in the formation of 2*H*-pyran-3(6*H*)-ones 3 and chromen-3(4*H*)-ones 4 upon facile trapping the vinyl cation intermediates by external N-oxide and internal aryl ring system.

Recently, gold-catalyzed oxidation of alkynes offered an expedient access to synthetically versatile α-oxo gold carbene intermediates to synthesize various useful molecules that display significant utility for chemical synthesis, medicines, and functionalized materials.[1] This strategy is safer and greener to construct C-X (X=C, N, O, S and Cl) bonds by internal/external nucleophiles trapping the in situ generated α-oxo gold carbenes, which circumvents the use of hazardous and potentially explosive α-diazo ketone precursors (eq 1).[2, 3] Various efficient synthetic methods have been developed by Zhang,[4, 5] Hashimi,[6] liu,[7] Ye, [8] Gagosz [9] and others [10] based on trapping α-oxo gold carbene intermediates. While, the alkyne as nucleophile trapped the α-oxo gold carbene intermediates generated in situ proves to be very challenging because of the selective of oxidation of diynes and other intractable side reactions. Recently Hashimi and co-workers have reported the gold catalyzed oxidation of 1,5-enediynes to indenones with internal alkynes trapping the gold carbenes through 1,6–carbene transfer intermediates (eq 2) [6c]. We envisioned that the α-oxo gold carbene intermediates were tapped by alkynes might alternatively have a *β*-C-gold vinyl cation [11] intermediates following by nucleophiles trapping (eq 3). To further develop alkynes as surrogates of hazardous α-diazo ketones in gold catalysis, we focused here on expanding the scope of suitable internal nucleophiles like alkynes. Our first target was 1,6-oxo-diynes (eq 4) and notably, the reaction, if developed, would offer a novel and rapid access to synthetically versatile 2*H*-pyran-3(6*H*)-ones **3** and chromen-3(4*H*)-ones **4** with N-oxide and aromatic ring trapping the *β*-C-gold vinyl cation intermediates. Meanwhile, the reaction would prove the *β*-C-gold vinyl cation intermediates experimentally.



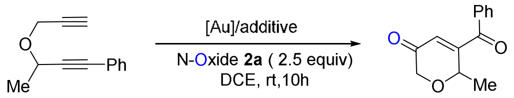
At the outset, we used 4-oxahepta-1,6-diyne **1a** and pyridine 1-oxide as the oxidant, and the results of reaction optimization are shown in Table 1. Initially, we started by using 0.3 mmol of **1a** and 2,6-dichloropyridine 1-oxide **2a** (2.5 equiv) with $Me_4{}^{t}BuXPhosAuCl$ (5 mol %)/ $NaBARF_4$ (10 mol %) as catalyst, to our delight, the double oxidation product of 5-benzoyl-6-methyl-2*H*-pyran-3(6*H*)-one **3a** was obtained in 82% isolated yield after 5 h in 1,2-dichloroethane (DCE) at room temperature (entry 1).[12] Other N-oxides were also investigated, like **2b-2e**, however no superior results were observed even after longer time (entries 2-5). The oxidant **2a** loading was also tested, no exciting results were

---

College of Science, Northwest A&F University 3 Taicheng Road, Yangling 712100, Shaanxi, China.
E-mail: *jikegong@nwsuaf.edu.cn*.

Electronic Supplementary Information (ESI) available: ^{1}H NMR, ^{13}C NMR and IR, HRMS of new compounds. For crystallographic data of **5** in CIF or other electronic format See DOI: 10.1039/x0xx00000x achieved (for details, see SI). While, decreased the gold catalyst loading to 2 mol % with 4 mol % $NaBARF_4$, an acceptable result (82 % yield) was observed after 10h (entry 6). Other cationic gold complexes derived from typical ligands such as Ph_3P, IPr were largely ineffective, thus resulting in 1, 6-diyne **1a** remaining with little desired product (entries 7-8). Mor-DalPhosAuNTf$_2$ (2 mol %) can also promote the reaction with less effective (entry 9). Solvent effect was also considered, such as acetone, acetonitrile and toluene, but no effective solvent was observed.

Table 1 Screening conditions [a]



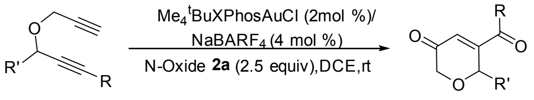
1a **3a**

Entry	Catalyst (mol %)	Additive (mol %)	Yield [b]
1	Me$_4{}^t$BuXPhosAuCl(5)	$NaBARF_4$ (10)	82% [c]
2	Me$_4{}^t$BuXPhosAuCl(5)	$NaBARF_4$ (10)	58% [d]
3	Me$_4{}^t$BuXPhosAuCl(5)	$NaBARF_4$ (10)	55% [e]
4	Me$_4{}^t$BuXPhosAuCl(5)	$NaBARF_4$ (10)	57% [f]
5	Me$_4{}^t$BuXPhosAuCl(5)	$NaBARF_4$ (10)	73% [g]
6	**Me$_4{}^t$BuXPhosAuCl(2)**	***$NaBARF_4$ (4)***	**82**%
7	Ph_3PAuCl(2)	$NaBARF_4$ (4)	< 3%
8	IPrAuCl(2)	$NaBARF_4$ (4)	<5%
9	Mor-DalPhosAuNTf$_2$(2)	-	72%
10	Me$_4{}^t$BuXPhosAuCl(2)	$NaBARF_4$ (4)	<3% [h]
11	Me$_4{}^t$BuXPhosAuCl(2)	$NaBARF_4$ (4)	45% [i]
12	Me$_4{}^t$BuXPhosAuCl(2)	$NaBARF_4$ (4)	<3% [j]

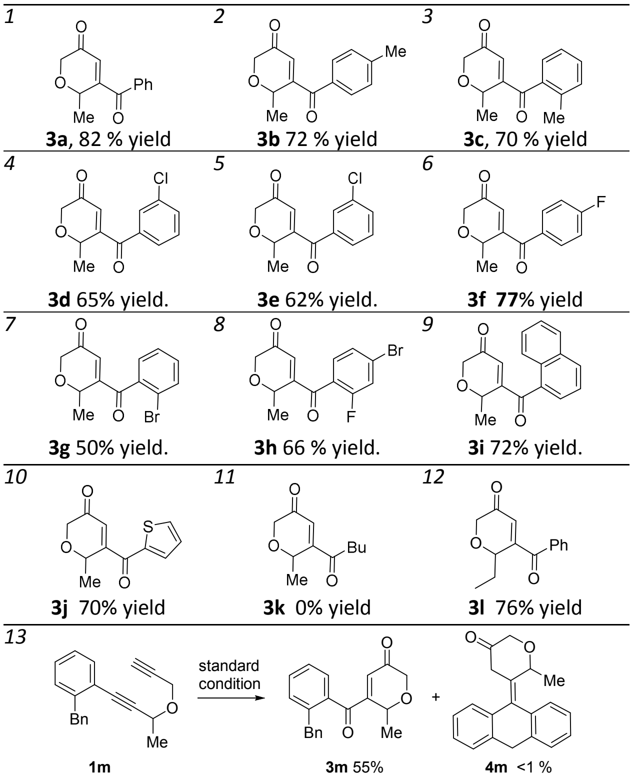
[a] The reaction was run with everything in a vial capped with a septum, Initially, [1a]=0.1M. [b] Isolated yield. [c] Reaction time 5h. [d] **2b** as The N-oxide. [e] **2c** as The N-oxide. [f] **2d** as The N-oxide. [g] **2e** as The N-oxide (for detail see SI). [h] Acetonitrile as the solvent. [i] Toluene as the solvent. [j] Acetone as the solvent.

With the optimized reaction conditions given in Table 1, entry 6, the scope of the transformation was first examined with various 4-oxahepta-1,6-diynes. As shown in Table 2. Thus, a tandem double oxidation of substituted 4-oxahepta-1,6-diynes **1a**-**m** except **1k** with one carbon-carbon double bond formation proceeded smoothly to provide corresponding products **2a**-**j** and **2l**-**m** in moderate to good yields. The reaction works well with aromatic **R** groups. Electron-donating aryl groups showed slight better results than those with an electron-withdrawing group in the reaction (**1b** vs **1d**). Various electron-withdrawing **R** group were tolerance. Steric effect of **R** aryl groups was also considered and the *o*-methyl aryl group showed better yield than *o*-bromide aryl group by installing the methyl and bromide group on *ortho* position (**1c** vs **1g**). 4-oxahepta-1,6-diyne **1j** with a heteroaromatic **R** group can also afford the desired product **2j** in 70% yield, while a substrate like **1k** with an aliphatic **R** group gave no reaction. It is reasonable to accept that the reaction needs a cation-stabilizing aryl group. Other 1,6-diyne like **1l** with different **R'** groups can also afford corresponding 2*H*-pyran-3(6*H*)-one **2l** in acceptable yield. 4-oxahepta-1,6-diyne **1m** with ortho-benzyl aryl **R** group was also investigated, a moderate yield of desired product **3m** was obtained. However, almost no **4m** was observed from crude NMR.

Table 2. Scope of 2*H*-pyran-3(6*H*)-ones 3.[a]



1 **3**



3a, 82 % yield

3b 72 % yield

3c, 70 % yield

3d 65% yield.

3e 62% yield.

3f **77**% yield

3g 50% yield.

3h 66 % yield.

3i 72% yield.

3j 70% yield

3k 0% yield

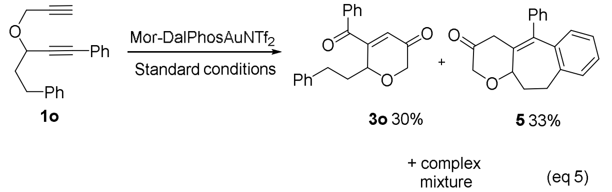
3l 76% yield

1m **3m** 55% **4m** <1 %

[a] Initially [1]=0.1M; The reactions were run under the standard conditions, unless otherwise specified. [b] Yields of isolated productsare shown.

Furthermore, to expand the scope of this reaction, we also investigated 4-oxahepta-1,6-diyne **1o** with 2 mol % of Mor-DalPhosAuNTf$_2$ as the catalyst by installing the ethylbenzene group on **R**' position. To our delight, the desired double oxidation product **3o** was obtained in 30% yield along with 5-phenyl-4,10,11,11a-tetrahydrobenzo[4,5]cyclohepta [1,2-*b*]pyran-3(2*H*)-one **5** in 33 % yield and some complex mixture (eq 5). The relative configuration of the product **5** was unambiguously assigned by X-ray crystallography. [13] For this phenomenon, we proposed that the phenyl ring trapped the vinyl cation intermediate as descript in eqs 4.

While considering synthetically useful transformations, we also sought to gather additional experimental evidence for the mechanism. To this end, we examined the direct conversion of 4-

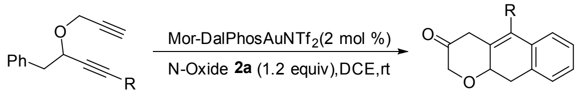


1o **3o** 30% **5** 33%

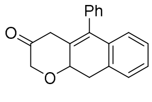
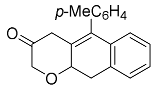
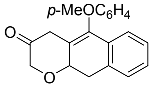
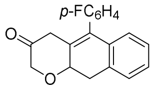
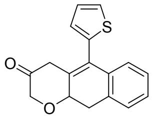
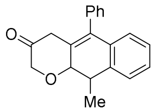
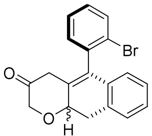
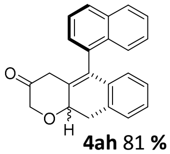
+ complex mixture (eq 5)

oxahepta-1,6-diynes **1aa-1ah** by installing the benzyl group on **R**′ position in the presence of 2 mol % of Mor-DalPhosAuNTf$_2$. Much to our delight, this strategy worked well with different substituents of **R** group affording various functionalized 10,10a-dihydro-2*H*-benzo[*g*]chromen-3(4*H*)-ones **4aa-4ah** in acceptable yield with two new C-C bonds formation as shown in Table 3. For the substrates **1ag-h** with an *o*-bromophenyl and naphthalene substituents, the reaction worked well and afforded the corresponding products **4ag-h** in 45% and 81% yield respectively with 5: 4 diastereoselectivity.

Table 3. Scope of 10,10a-dihydro-2*H*-benzo[*g*]chromen-3(4*H*)-ones 4.[a]



1aa-1ah **4aa-4ah**

1  **4aa**, 63% yield	2  **4ab** 58 % yield	3  **4ac**, 56 % yield
4  **4ad**, 55 % yield	5  **4ae** 76 **%** yield	6  **4af**, 75 % yield
7  dr=5:4 **4ag** 45 % yield	8  dr=5:4 **4ah** 81 **%** yield	

[a] Initially [1]=0.1M; The reactions were run under the standard conditions, unless otherwise specified. [b] Yields of isolated products are shown.

An interesting phenomenon was observed when 4-oxahepta-1,6-diyne **1p** was investigated in this reaction. The product 6,6-dimethyl-5-phenyl-5,6,7,7a-tetrahydrocyclopenta[b]pyran-3(2*H*)-one **6** was obtained in 80% yield. We proposed that the reaction was occurred through the vinyl cation intermediate and 1,5-H migration[14] process to afford **6** (Fig 1). This case is an additional experimental evidence for the vinyl cation intermediates.

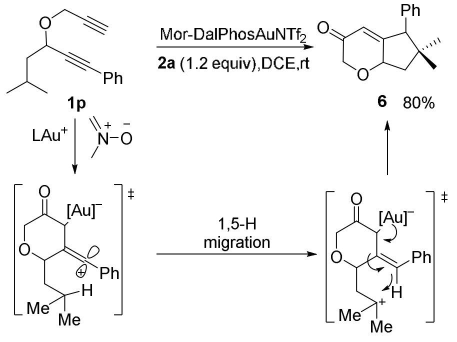


Fig. 1 Proposed mechanism to pyran-3(2*H*)-one **6**

On the basis of the above observations, we propose the following plausible mechanisms for this transformation (Fig 2). i) Coordination of the diynes moiety with the cationic gold complexes and N-oxide selectively attacked the terminal alkyne to give the complexes **A**. ii) The gold complexes backed donation the electron to remove the 2,6-dichloropyridine and gave the α-oxo gold carbene intermediates **B,** followed by internal alkynes attacking to form the vinyl cation intermediates **C**. iii) The vinyl cation intermediates **C** were trapped by external N-oxide to form the intermediates **D** followed by removing the 2,6-dichloropyridine to give **3.** Alternatively**,** if **R′** contained an aryl ring in suitable position, the vinyl cation intermediates **C** might be trapped by internal aryl ring to give products **4**.

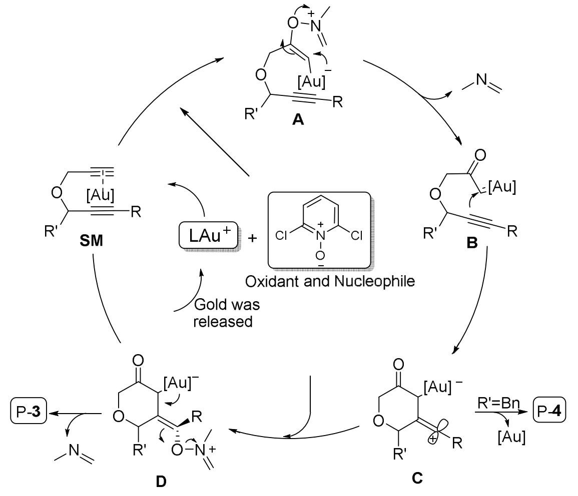


Fig. 2 Proposed Mechanism

In summary, we have described a gold-catalyzed selectively oxidation of 4-oxahepta-1,6-diynes to various 2*H*-pyran-3(6*H*)-ones **3** and 10,10a-dihydro-2*H*-benzo[*g*]chromen-3(4*H*)-ones **4** in the presence of 2 mol % catalyst loading. We also observed the interesting product **6** with 1,5-H migration. The reaction proceeded smoothly to provide corresponding products through the α-oxo gold carbene intermediates generated in situ and β-C-gold vinyl cation intermediates which can be trapped by external N-oxide and internal aryl ring systems. A more detailed investigation on the mechanism, as well as the scope of this cascade, is ongoing in our laboratory.

We are grateful for the financial support from Northwest A&F University (Z111021404)

Notes and references

1. L. Ye, L. Cui, G. Zhang and L. Zhang, *J. Am. Chem. Soc.*, **2010**, *132*, 3258–3259.
2. For a monograph, see: M. P. Doyle, M. A. McKervey and T. Ye, Modern catalytic methods for organic synthesis with diazo

compounds: from cyclopropanes to ylides, Wiley, New York, 1998.

3. For examples of gold carbenes generated from α-diazo carbonyl compounds, see: (a) M. R. Fructos, T. R. Belderrain, P. de Fremont, N. M. Scott, S. P. Nolan, M. M. Diaz-Requejo and P. J. Perez, *Angew. Chem., Int. Ed.*, **2005**, *44*, 5284–5288; (b) A. Prieto, M. R. Fructos, M. Mar Díaz-Requejo, P. J. Pérez, P. Pérez-Galán, N. Delpont and A. M. Echavarren, *Tetrahedron*, **2009**, *65*, 1790–1793; (c) S. K. Pawar, C.-D. Wang, S. Bhunia, A. M. Jadhav and R.-S. Liu, *Angew. Chem., Int. Ed.*, **2013**, *52*, 7559–7563; (d) V. V. Pagar, A. M. Jadhav and R.-S. Liu, *J. Org. Chem.*, **2013**, *78*, 5711–5716; (e) A. M. Jadhav, V. V. Pagar and R.-S. Liu, *Angew. Chem., Int. Ed.*, **2012**, *51*, 11809–11813; (f) Z.-Y. Cao, X. Wang, C. Tan, X.-L. Zhao, J. Zhou and K. Ding, *J. Am. Chem. Soc.,* **2013**, *135,* 8197–8200. (g)Z. Yu, B. Ma, M. Chen, H. Wu, L. Liu and J. Zhang, *J. Am. Chem. Soc.* **2014***, 136,* 6904-6907.
4. For selected examples (a) B. Lu, C. Li and L. Zhang, *J. Am. Chem. Soc.*, **2010**, *132*, 14070–14072; (b) L. Ye, W. He and L. Zhang, *J. Am. Chem. Soc*., **2010**, *132*, 8550–8551; (c) W. He, C. Li and L. Zhang, *J. Am. Chem. Soc*., **2011**, *133*, 8482–8485; (d) L. Ye, W. He and L. Zhang, *Angew. Chem., Int. Ed.,* **2011**, *50*, 3236–3239; (e) Y. Wang, K. Ji, S. Lan and L. Zhang, *Angew. Chem., Int. Ed*., **2012**, *51*, 1915–1918; (f) Y. Luo, K. Ji, Y. Li and L. Zhang, *J. Am. Chem. Soc*., **2012**, *134*, 17412–17415; (g) K. Ji, Y. Zhao and L. Zhang, *Angew. Chem., Int. Ed.*, **2013**, *52*, 6508–6512; (h) K. Ji, J. Nelson and L. Zhang, *Beilstein J. Org. Chem.*, **2013**, *9*, 1925–1930; (i) L. Zhang, *Acc. Chem. Res*., 2014,47,877-888; (j) K. Ji, Z. Zheng, Z. Wang, L. Zhang, *Angew. Chem. Int. Ed.;* **2015,** 54, 1245-1249.
5. For selected examples (a) D. Qian, H. Hu, F. Liu, B. Tang, W. Ye, Y. Wang and J. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 13751-13755; (b) D. Qian, J. Zhang. *Chem. Commun.* **2012**, *48*, 7082-7084; (c) D. Qian, J. Zhang, *Chem. Commun.* **2011**, *47*, 11152-11154.
6. For selected examples (a) A. S. K. Hashmi, T. Wang, S. Shi and M. Rudolph, *J. Org. Chem*., **2012**, *77*, 7761–7767;(b) S. Shi, T. Wang, W. Yang, M. Rudolph and A. S. K. Hashmi, *Chem. Eur. J*., **2013**, *19*, 6576–6580. (c) P. Nösel, L. N. S. Comprido , T. Lauterbach, M. Rudolph, F. Rominger, and A. S. K. Hashmi , *J. Am. Chem. Soc.*, **2013**, *135*, 15662–15666.
7. For selected examples (a) C.-W. Li, G. -Y. Lin and R. -S. Liu, *Chem. Eur. J.*, **2010**, *16*, 5803–5811; (b) C.-W. Li, K. Pati, G.-Y. Lin, S. M. A. Sohel, H.-H. Hung and R.-S. Liu, *Angew. Chem., Int. Ed*., **2010**, *49*, 9891–9894; (c) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das and R. -S. Liu, *Angew. Chem., Int. Ed*., **2011**, 50, 6911–6914.
8. For selected examples (a) C. Shu, R.-F. Liu, S. Liu**,** J.-Q. Li, Y.-F. Yu, Q. He, X. Lu, L.-W. Ye, *Chem. Asian. J.* **2015**, *1*, 91-95. (b) F. Pan, S. Liu, C. Shu, R.-K. Lin, Y.-F. Yu, J.-M. Zhou, L.-W. Ye, *Chem. Commun*. **2014**, *50*, 10726-10729.
9. For selected example: G. Henrion, T. E. J. Chavas, X. Le Goff and F. Gagosz, *Angew. Chem., Int. Ed*., **2013**, *52*, 6277–6282.
10. For selected examples done by other researchers, see: M. Xu, T.-T. Ren and C. -Y. Li, *Org. Lett*., **2012**, *14*, 4902–4905; (b)) P. W. Davies, A. Cremonesi and N. Martin, *Chem. Commun*., **2011**, *47*, 379–381; (c) M. Chen, Y. Chen, N. Sun, J. Zhao, Y. Liu, Y. Li, *Angew. Chem. Int. Ed.;* **2015,** 54, 1200-1204.
11. M. Hanack, *Acc. Chem. Res.*, **1976**, *9*, 364–371; (b) M. Hanack, *Acc. Chem. Res.,* **1970**, *3*, 209–216; (c) T. Okuyama, *Acc. Chem. Res.*, **2002**, *35*, 12–18.

12 For in situ generated Rhodium(I) carbenes from ynamides and their Reactions with alkynes see: R. Liu, G. N. Winston-McPherson, Z.-Y. Yang, X. Zhou, W. Song, I. A. Guzei, X. Xu, W. Tang *J. Am. Chem. Soc.* **2013**, *135*, 8201−8204.

13. For X-ray structure of **5**, The CCDC number is 1058971.
14. For examples of 1,5-hydride shifts observed in gold(I)-catalyzed processes, see: (a) Y. Harrak, A. Simonneau, M. Malacria, V. Gandon, L. Fensterbank, *Chem. Commun.* **2010**, *46*, 865-867; (b) E. Jiménez-Núñez, M. Raducan, T. Lautenbach, K. Molawi, C. R. Solorio, A. M. Echavarren, *Angew. Chem., Int. Ed.* **2009**, *48*, 6152-6155; (c) Li. Cui, Y. Peng, L. Zhang, *J. Am. Chem. Soc*. **2009**, *131*, 8394-8395; (d) S. Bhunia, R.-S. Liu, *J. Am. Chem. Soc*. **2008**, *130*, 16488-16489. (e) G. Zhou, J. Zhang, *Chem. Commun.* **2010**, *46*, 6593-6595; (f) B. Bolte and F. Gagosz, *J. Am. Chem. Soc.*, **2011**, *133*, 7696–7699.