ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2014, **50**, 2158

Received 10th December 2013,
Accepted 24th December 2013

DOI: 10.1039/c3cc49351b

www.rsc.org/chemcomm

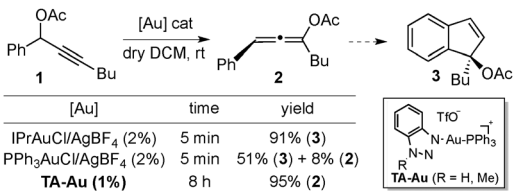
Quantitative kinetic investigation of triazole–gold(I) complex catalyzed [3,3]-rearrangement of propargyl ester†

Yumeng Xi,[a] Qiaoyi Wang,[a] Yijin Su,[a] Minyong Li*[b] and Xiaodong Shi*[a]

The triazole–gold(I) complex catalyzed [3,3]-rearrangement of propargyl ester has been quantitatively investigated through *in situ* IR. First order dependence of the initial rates on [Au] and [propargyl ester] suggested that the turnover-limiting step is the associative ligand substitution. The activation enthalpy was also determined to be 7.8 kcal mol^{-1}. TA–Au catalysts with different triazole derivatives were also tested, giving a linear free energy relationship with a ρ value of 0.74.

The past decade has witnessed the fast growing homogenous gold catalysis.[1] Compared with the fast pace of new transformation development, the mechanistic investigations are left much behind. Meanwhile, with recent efforts to characterize catalytic intermediates using X-ray crystallography and NMR,[2] more and more evidence suggests that a much more complicated mechanism is operative in real case rather than the oversimplified mechanism previously assumed. Furthermore, the recent observation of the "silver effect",[3] Au–Cl–Ag[4] and Au–Cl–Au[5] complexes, and "small gold cluster" catalysis[6] further supports the more complex mechanism, and stimulates the need for a mechanistic study. In general, gold catalysis involves three important steps: coordination (to alkyne/alkene), protodeauration and gold decomposition (side reaction).[7] Thus, due to the mechanistic complexity (especially the existence of fast decomposition), efforts to target each elementary step in the catalytic cycle are not always fruitful.[8] Thanks to the recent mechanistic studies from several laboratories, meaningful data were derived from some stoichiometric reactions,[9] although they may not necessarily reflect the catalytic reactions accurately.

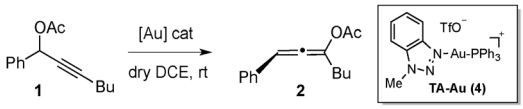
In 2009, our group introduced a 1,2,3-triazole bound cationic gold(I) complex (TA–Au) as an improved thermally stable catalyst.[10] Later it was discovered that the TA–Au complex could preferentially activate alkyne over allene in propargyl ester [3,3]-rearrangement,[11] where indene was synthesized using 2 mol% IPrAuCl/AgBF$_4$ (Scheme 1).[12] However, in our case, no indene was detected after 12 h using 1 mol% TA–Au. We view this phenomenon as a good opportunity for the mechanistic study. The simplified system (over Nolan's two-step transformation) may allow for the collection of quantitative kinetic information associated with TA–Au. In addition, it is also very important to understand why TA–Au offered the chemoselectivity with excellent stereochemistry control, while other [L–Au]$^+$ complexes led to rapid racemization at the propargyl position with poor chemoselectivity (activation of both alkyne and allene). Herein, we report our quantitative kinetic investigation of TA–Au catalyzed propargyl ester [3,3]-rearrangement using *in situ* IR spectroscopy from a 'live' catalytic reaction.[13]



[Au]	time	yield
IPrAuCl/AgBF$_4$ (2%)	5 min	91% (**3**)
PPh$_3$AuCl/AgBF$_4$ (2%)	5 min	51% (**3**) + 8% (**2**)
TA-Au (1%)	8 h	95% (**2**)

Scheme 1 TA–Au as a chemoselective catalyst for alkyne activation.

To acquire meaningful kinetic data for a catalytic reaction, the turnover-limiting step needs to be established. This is a challenging task for the LAuCl–AgX system, leading to the rapid catalyst decomposition over time. A unique advantage of the TA–Au catalyst is its improved stability, which allows relatively steady concentration of the catalyst for the kinetic study. Thus, we set out to evaluate the kinetic dependence of concentration of the substrate and TA–Au. The standard reaction was chosen as the model reaction for the detailed investigation (eqn (1)).



(1)

To avoid the potential influence of acid (formation of HOTf), the *N*-Me-benzotriazole (instead of N–H) coordinated TA–Au **4** was selected.[14] The dependence of the initial rates on the

[a] *C. Eugene Bennett Department of Chemistry, West Virginia University, Morgantown, WV 26506, USA. E-mail: Xiaodong.Shi@mail.wvu.edu; Fax: +1-304-293-4904; Tel: +1-304-293-0179*

[b] *Department of Medicinal Chemistry, School of Pharmacy, Shandong University, Jinan, Shandong, 250012, China. E-mail: mli@sdu.edu.cn*

† Electronic supplementary information (ESI) available: Experimental procedures, and kinetic and DFT data. See DOI: 10.1039/c3cc49351b

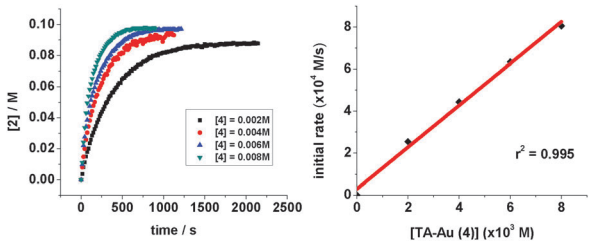


Fig. 1 Dependence of the initial rates on catalyst concentrations for rearrangement of **1**. Reaction conditions: **1** (0.10 M in DCE, 1.2 mL), **4** (0.002–0.008 M in DCE), 30 °C.

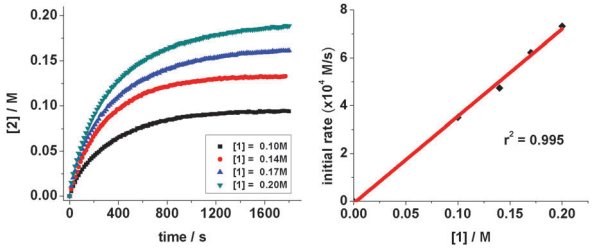


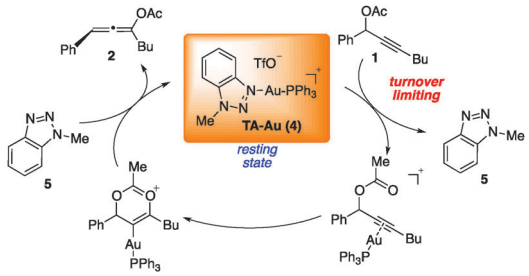
Fig. 2 Dependence of the initial rates on substrate concentrations for rearrangement of **1**. Reaction conditions: **1** (0.10–0.20 M in DCE, 1.2 mL), **4** (0.003 M in DCE), 30 °C.

concentration of TA–Au catalyst **4** was studied with varied concentrations from 0.002–0.008 M. The initial rates in different runs were calculated based on the kinetic profiles monitored by *in situ* IR. A linear relationship is established as depicted in Fig. 1. The reaction is therefore first-order dependent on [**4**], suggesting the involvement of **4** in the turnover-limiting step.

A subsequent experiment was performed to determine the kinetic order of [**1**]. Similarly, the initial rates were plotted against [**1**] varied from 0.10–0.20 M. Again, a first-order dependence was observed, as shown in Fig. 2. Combining the two experiments, we were able to derive the rate law for this reaction: $r = k_{obs}[\mathbf{1}]^1[\mathbf{4}]^1$. According to the rate law, both the catalyst **4** and substrate **1** were involved, revealing the electronic activation of alkyne (*i.e.* ligand exchange) as the turnover-liming step. *In situ* monitoring by ^{31}P NMR over the entire course of reaction showed **4** as the resting state further supporting the ligand exchange as the turnover-limiting step.

With these kinetic data, a tentatively proposed mechanism of TA–Au catalyzed propargyl ester [3,3]-rearrangement is shown in Scheme 2. First, the TA–Au complex undergoes the turnover-limiting ligand exchange with the substrate to form the cationic gold(I) alkyne π-complex. This complex then rapidly converts the propargyl ester to the corresponding allene. It is clearly seen that the ligand exchange step significantly slows the reaction rate compared to the use of free cationic gold(I) (Scheme 1), which is consistent with the fact that the same reaction catalyzed by IPrAu(L)$^+$ (L = Et_3N, py) was also slower.[15]

To further probe the physical organic nature of this elementary step, a temperature dependent experiment was carried out in order to obtain the activation energy quantitatively. As shown in Fig. 3, the reactions were again monitored by *in situ* IR at different temperatures (295–319 K). The activation enthalpy was determined to be 7.8 kcal mol^{-1} through the Erying equation after plotting the $\ln(k_{obs}/T)$ *vs.* $1/T$. This value reveals that the ligand exchange step



Scheme 2 Proposed mechanism for TA–Au catalyzed propargyl ester [3,3]-rearrangement.

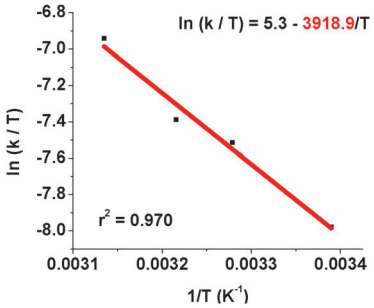
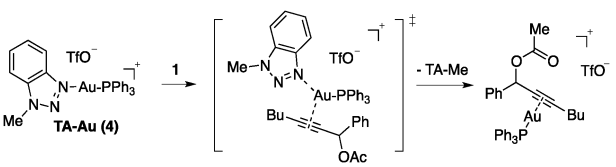


Fig. 3 Kinetics profile at different temperatures. Reaction conditions: **1** (0.10 M in DCE, 1.2 mL), TA–Au (0.003 M in DCE), at 22, 32, 38, and 46 °C.

itself is quite a facile process at room temperature. Similarly, Echavarren reported even lower activation enthalpy values (3.7 and 6.2 kcal mol^{-1}) in his studies on the enyne cycloisomerization.[16]

Assuming that all the catalyst in the reaction remained active throughout the reaction, $[\mathbf{4}]_0$ will be identical to active catalyst concentration. Therefore, activation entropy was determined to be −36.6 eu. This negative and relatively large value supports the associative ligand substitution through a transient 3-coordinate gold(I) complex. However, the possibility of the 3-coordinate gold(I) complex with TA attached as the stable intermediate cannot be ruled out at this point. Further support came from the fact that the reaction was inhibited if additional 1-methyl-benzotriazole (**5**, 4 equiv. toward TA–Au) was present. Unfortunately, we were unable to determine the exact order of [**5**] due to the extremely slow reaction rates. But a negative kinetic order of [**5**] is anticipated, which is consistent with the proposed triazole–alkyne exchange mechanism shown in Scheme 3.[17]

Finally, we prepared various TA–Au catalysts with different substituted benzotriazoles in order to investigate the impact of the electronic nature of the TA–Au catalysts.[18] The ^{31}P NMR peaks corresponding to TA–Au catalysts provide direct information regarding the electronic nature of the gold center. As expected, a more electron-withdrawing group gives a more upfield ^{31}P shift,



Scheme 3 Associative ligand substitution through a transient 3-coordinate cationic gold(I) complex.

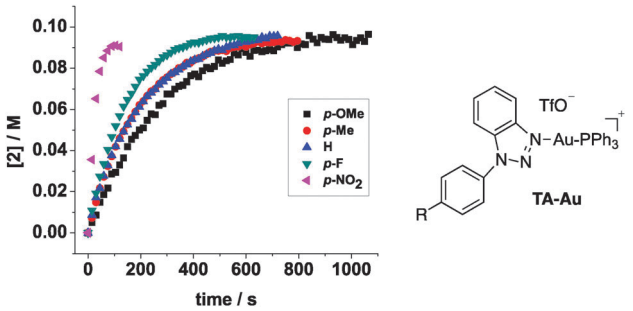


Fig. 4 Kinetics profile using various TA–Au catalysts. Reaction conditions: **1** (0.10 M in DCE, 1.2 mL), TA–Au (0.003 M in DCE), 26 °C.

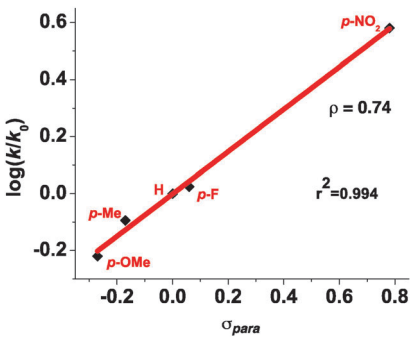


Fig. 5 Hammett plot of various TA–Au catalysts.

suggesting the more cationic gold. The reaction kinetics is illustrated in Fig. 4.

Clearly, the more cationic gold(I) led to a faster reaction rate. The slowest reaction was observed with the 4-methoxyphenyl substituted TA–Au catalyst, however, this reaction is still faster than the reaction catalyzed by **4**, suggesting the inherent electron-withdrawing nature of the phenyl group attached to benzotriazole. The linear free energy relationship was established by plotting $\log(k/k_H)$ *vs.* σ_{para}, giving a ρ value of 0.74 (Fig. 5).

The positive ρ value suggested partial positive charge building up during the reaction, which is consistent with the associative ligand substitution being the turnover-limiting step. The more electron-deficient triazole undergoes ligand exchange more rapidly, which is accounted for by the faster reaction rate. This result also highlights the tunability of the TA–Au catalyst. Based on the different cases, the more electron-deficient TA–Au will give a shorter reaction time, while the more electron-rich TA–Au has a longer catalyst lifetime.

The chemoselectivity of the TA–Au catalysts (activation of alkyne over allene) can also be explained by this ligand–substrate exchange mechanism. The DFT calculation revealed that the HOMO of propargyl ester **1** is 20 kcal mol^{-1} higher than the HOMO of allene **2**.[19] Thus, the ligand exchange is much slower between allene and TA–Au, which supports the observed selective alkyne activation.[20]

In summary, the triazole–gold(I) complex (TA–Au) catalyzed propargyl ester [3,3]-rearrangement has been quantitatively investigated. Considering that few physical organic studies have been reported regarding gold catalyzed alkyne activation due to the poor catalyst stability and complex reaction nature, this work provided direct experimental evidence for understanding the elementary step in the TA–Au catalyzed alkyne activation. The discovery of associative ligand exchange between TA–Au and alkyne as the turnover-limiting step provided mechanistic insight, which will benefit future investigations.

We thank the NSF (CAREER-CHE-0844602 and CHE-1228336) and NSFC (No. 21228204) for financial support.

Notes and references

1 (*a*) A. S. K. Hashmi and F. D. Toste, *Modern Gold Catalyzed Synthesis*, Wiley-VCH, Weinheim, 2012; (*b*) A. S. K. Hashmi and M. Rudolph, *Chem. Soc. Rev.*, 2012, **41**, 2448; (*c*) D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351; (*d*) A. Arcadi, *Chem. Rev.*, 2008, **108**, 3266; (*e*) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326; (*f*) A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180; (*g*) A. Fürstner and P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410; (*h*) L. Zhang, J. Sun and S. A. Kozmin, *Adv. Synth. Catal.*, 2006, **348**, 2271; (*i*) A. S. K. Hashmi and G. J. Hutchings, *Angew. Chem., Int. Ed.*, 2006, **45**, 7896.

2 For recent reviews, see: (*a*) A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2010, **49**, 5232; (*b*) L. Liu and G. B. Hammond, *Chem. Soc. Rev.*, 2012, **41**, 3129; (*c*) R. E. M. Brooner and R. A. Widenhoefer, *Angew. Chem., Int. Ed.*, 2013, **52**, 11714.

3 (*a*) D. Weber and M. R. Gagné, *Org. Lett.*, 2009, **11**, 4962; (*b*) D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen and X. Shi, *J. Am. Chem. Soc.*, 2012, **134**, 9012.

4 (*a*) S. G. Weber, F. Rominger and B. F. Straub, *Eur. J. Inorg. Chem.*, 2012, 2863; (*b*) Y. Zhu, C. S. Day, L. Zhang, K. J. Hauser and A. C. Jones, *Chem.–Eur. J.*, 2013, **19**, 12264.

5 A. Homs, I. Escofet and A. M. Echavarren, *Org. Lett.*, 2013, **15**, 5782. References cited therein.

6 (*a*) J. Oliver-Meseguer, J. R. Cabrero-Antonino, I. Domínguez, A. Leyva-Pérez and A. Corma, *Science*, 2012, **338**, 1452; (*b*) J. Oliver-Meseguer, A. Leyva-Pérez and A. Corma, *ChemCatChem*, 2013, **5**, 3509.

7 W. Wang, G. B. Hammond and B. Xu, *J. Am. Chem. Soc.*, 2012, **134**, 5697.

8 For representative studies, see: (*a*) Z. J. Wang, D. Benitez, E. Tkatchouk, W. A. Goddard III and F. D. Toste, *J. Am. Chem. Soc.*, 2010, **132**, 13064; (*b*) T. J. Brown, D. Weber, M. R. Gagné and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2012, **134**, 9134.

9 (*a*) T. J. Brown, M. G. Dickens and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2009, **131**, 6350; (*b*) T. J. Brown, A. Sugie, M. G. D. Leed and R. A. Widenhoefer, *Chem.–Eur. J.*, 2012, **18**, 6959; (*c*) R. E. M. Brooner, T. J. Brown and R. A. Widenhoefer, *Chem.–Eur. J.*, 2013, **19**, 8276.

10 H. Duan, S. Sengupta, J. L. Petersen, N. G. Akhmedov and X. Shi, *J. Am. Chem. Soc.*, 2009, **131**, 12100.

11 (*a*) D. Wang, L. N. S. Gautam, C. Bollinger, A. Harris, M. Li and X. Shi, *Org. Lett.*, 2011, **13**, 2618; (*b*) D. Wang, X. Ye and X. Shi, *Org. Lett.*, 2010, **12**, 2088–2091.

12 (*a*) N. Marion, S. Díez-Gonzalez, P. Fremont, A. R. Noble and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2006, **45**, 3647; and for an early example, see: (*b*) L. Zhang and S. Wang, *J. Am. Chem. Soc.*, 2006, **128**, 1442.

13 (*a*) C. He, J. Ke, H. Xu and A. Lei, *Angew. Chem., Int. Ed.*, 2013, **52**, 1527; (*b*) Z. Huang, L. Jin, H. Han and A. Lei, *Org. Biomol. Chem.*, 2013, **11**, 1810; (*c*) J. Li, L. Jin, C. Liu and A. Lei, *Chem. Commun.*, 2013, **49**, 9615.

14 D. Wang, Y. Zhang, A. Harris, L. N. S. Gautam and X. Shi, *Adv. Synth. Catal.*, 2011, **353**, 2584.

15 P. Nun, S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 9113.

16 C. Nieto-Oberhuber, S. López, M. P. Muñoz, D. J. Cárdenas, E. Buñuel, C. Nevado and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2005, **44**, 6146.

17 The inhibition could be explained by either the formation of 3-coordinate $LAu(TA)_2^+$-type complex or the competition of the external triazole ligand with alkyne substrate. Unfortunately, our attempts to detect the 3-coordinate gold complex through MS and NMR were unfruitful with no observation of any $LAu(TA)_2^+$ type complexes. Thus, the equilibrium between TA–Au and Au–alkyne π-complex is the likely explanation for the observed decreased reaction rate when external TA ligands were used. Detailed derivation of rate law is provided in ESI†.

18 K. Wang, M. Chen, Q. Wang, X. Shi and J. K. Lee, *J. Org. Chem.*, 2013, **78**, 7249.

19 DFT calculation was performed on Gaussian 03 program at the B3LYP/6-311G level of theory.

20 P. Nun, S. Gaillard, A. Poater, L. Cavalloc and S. P. Nolan, *Org. Biomol. Chem.*, 2011, **9**, 101.

