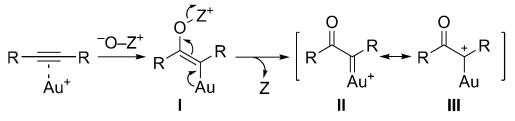
Synthetic Methods

DOI: 10.1002/ange.201304700

Gold-Catalyzed Oxidative Rearrangement Involving 1,2-Acyl Migration: Efficient Synthesis of Functionalized Dihydro-γ-Carbolines from α-(2-Indolyl) Propargylic Alcohols and Imines**

*Lu Wang, Xin Xie, and Yuanhong Liu**

In recent years, gold-catalyzed oxidative reactions of alkynes have received considerable attention, since they provide efficient access to functionalized carbo- and heterocycles.[1–4] Usually, the reaction is initiated by the attack of a nucleophilic oxygen atom of the oxidant on the gold-activated alkyne; this step is followed by the elimination of a neutral organic framework with concomitant formation of α-carbonyl gold carbenoid **II/III** (Scheme 1). The gold carbenoid generated in these reactions could undergo further reactions with various

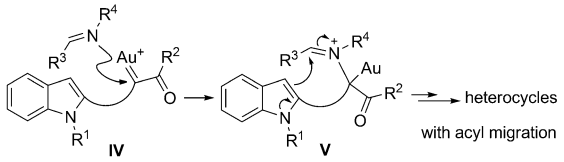


$^{-}O–Z^{+}$ = pyridine *N*-oxide, quinoline *N*-oxide, diphenyl sulfoxide, nitrones, etc.

Scheme 1. Generation of an α-carbonyl gold carbenoid.

nucleophiles owing to its high electrophilicity and could therefore serve as a promising intermediate in the 1,2-difunctionalization of alkynes. Although much progress has been made in this area, most studies have relied on the intramolecular trapping of the gold carbenoid intermediate, whereas intermolecular reactions of these highly reactive gold species with external nucleophiles are quite rare, presumably as a result of the competitive attack of these nucleophiles on the alkyne substrate, reaction of the reduced form of the oxidant with the gold carbenoid, and undesired intramolecular reactions, such as a 1,2-hydride shift. Zhang and co-workers have reported a gold-catalyzed synthesis of oxazoles based on the trapping of α-carbonyl gold carbenoids with nitriles used as the solvent.[5] They have also shown that a P,N or P,S bidentate ligand can be used to temper the reactivity of gold carbenoids in gold-catalyzed [3+2] annulations of terminal alkynes with carboxamides.[6] Liu and co-workers developed a gold-catalyzed 1,2-difunctionalization of amino-alkynes by the use of nitrones. In these reactions, the imine formed as a putative intermediate acted as a nucleophile to attack the gold carbenoid in a cascade fashion.[7] Nevertheless, the trapping of these active gold carbenoid intermediates with external nucleophiles derived from readily available starting materials is still highly challenging.

Indoles are very important building blocks in organic synthesis and can be viewed as excellent nucleophiles for electrophilic substitution reactions owing to the π-excessive nature of the indolyl aromatic ring. During our ongoing investigations into gold-catalyzed cascade reactions of indole-alkynes,[8] we envisioned that the use of indolyl-tethered alkynes might lead to the α-carbonyl gold carbenoid **IV** in the presence of gold and an oxidant. This carbenoid might react intermolecularly with nucleophiles, such as imines, to generate an iminium cation **V**, which in turn could react with the indole moiety at its C3 position to form a new ring (Scheme 2). In this design, the imine also plays an important role as both the nucleophile and the electrophile. Herein, we report a gold-catalyzed oxidative rearrangement of α-(2-indolyl) propargyl alcohols with imines. This reaction enables the efficient construction of functionalized dihydro-γ-carbolines under mild reaction conditions with high regioselectivity. Most strikingly, an intriguing gold-assisted 1,2-acyl migration occurs during the process. To our knowledge, such a migration is unprecedented.



Scheme 2. Strategy for gold-catalyzed alkyne oxidation with external nucleophiles.

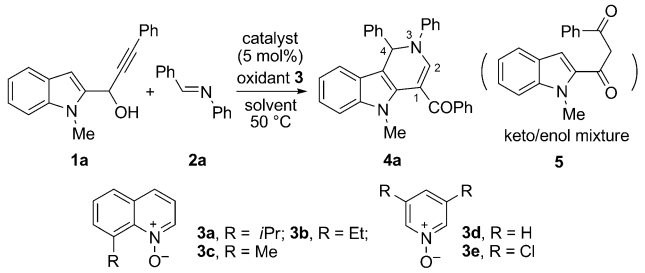
Initially, reactions of the 1-(*N*-methyl-2-indolyl)propargyl alcohol **1a** with imine **2a** in the presence of various gold catalysts and quinoline or pyridine *N*-oxides **3** were investigated for optimization of the reaction conditions (Table 1). Gratifyingly, the use of 8-isopropylquinoline *N*-oxide (**3a**) as the oxidant and [JohnPhos(MeCN)Au]SbF_6 (**A**) as the catalyst in 1,2-dichloroethane (DCE) resulted in the formation of dihydro-γ-carboline **4a** in 66% yield after 2 h (Table 1, entry 1).[9] To our surprise, **4a** was not the expected 2-acyl dihydro-γ-carboline, but instead the 1-acyl dihydro-γ-carboline, according to X-ray crystal-structure analysis of the analogous products **4c**, **4e**, **4k**, **4v**, and **4w** (see below).[10] The

[*] L. Wang, X. Xie, Prof. Y.-H. Liu
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
345 Lingling Lu, Shanghai 200032 (P. R. China)
E-mail: yhliu@mail.sioc.ac.cn

[**] We thank the National Natural Science Foundation of China (Grant Nos. 21121062, 21125210), the Chinese Academy of Sciences, and the Major State Basic Research Development Program (Grant No. 2011CB808700) for financial support. We also thank Dr. Guoqin Fan and Kebin Mao for the preparation of some imines.

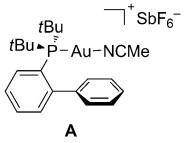
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201304700.

Table 1: Optimization studies for the formation of dihydro-γ-carboline **4a**.



Entry	**1a**/**2a**/**3**	Oxidant	Catalyst	Solvent	*t* [h]	Yield [%][a]
1	1.3 : 1 : 1.4	**3a**	**A**	DCE	2	66
2	1.3 : 1 : 1.4	**3a**	**A**	THF	5	55
3	1.3 : 1 : 1.4	**3a**	**A**	CH_3CN	3	59
4	1.3 : 1 : 1.4	**3a**	**A**	toluene	2	74
5	1.3 : 1 : 1.4	**3b**	**A**	toluene	2	71
6	1.3 : 1 : 1.4	**3c**	**A**	toluene	6	56
7	1.3 : 1 : 1.4	**3a**	[JohnPhosAu]SbF_6[b]	toluene	3	58
8	1.3 : 1 : 1.4	**3a**	[PPh_3Au]SbF_6	toluene	6	60
9	1.3 : 1 : 1.4	**3a**	[PPh_3Au]NTf_2	toluene	2	78
10[c]	1.3 : 1 : 1.4	**3a**	[PPh_3Au]NTf_2	toluene	2	88[d]
11[c,e]	1.3 : 1 : 1.4	**3a**	[PPh_3Au]NTf_2	toluene	2	84
12[c]	1.1 : 1 : 1.2	**3a**	[PPh_3Au]NTf_2	toluene	2	74
13[c]	1.3 : 1 : 1.4	**3d**	[PPh_3Au]NTf_2	toluene	3	76
14[c]	1.3 : 1 : 1.4	**3e**	[PPh_3Au]NTf_2	toluene	24	42
15	1.3 : 1 : 1.4	**3a**	[PPh_3AuCl]	toluene	2	NR[f]
16	1.3 : 1 : 1.4	**3a**	$AgNTf_2$	toluene	6	–[g]
17[c]	1.3 : 1 : 0	–	[PPh_3Au]NTf_2	toluene	6	–[h]

[a] Yield of isolated **4a** as based on the imine substrate. All reactions were carried out on a 0.2 mmol scale. [b] JohnPhos = (2-biphenyl)di-*tert*-butylphosphine. [c] Molecular sieves (4 Å; 50 mg) were added. [d] Product **5** was isolated in 10% yield based on substrate **1a**. [e] The reaction was carried out at room temperature. [f] No reaction was observed. [g] The reaction was not clean; **1a** was recovered in 47% yield. [h] The reaction was not clean; **1a** was recovered in 34% yield. Tf = trifluoromethanesulfonyl.

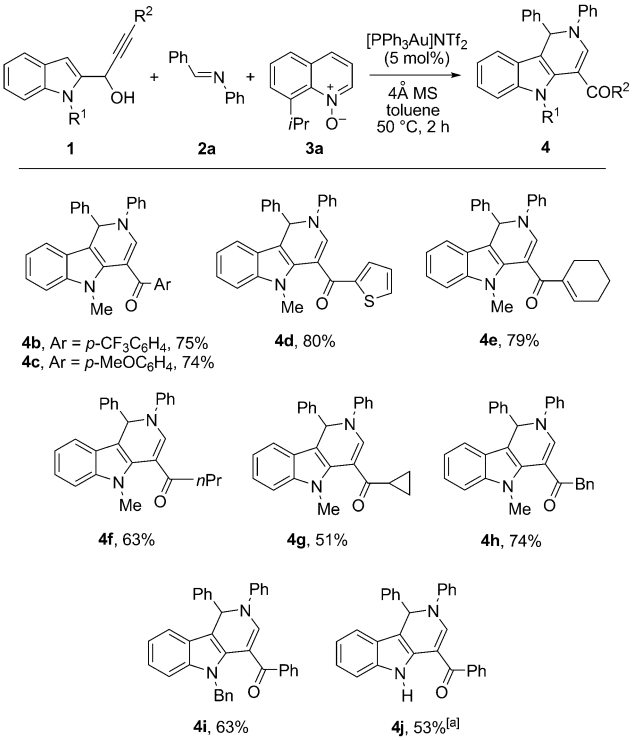


A

results indicated that an unusual acyl migration occurred during the reaction process. When the solvent was changed to THF or CH_3CN, lower yields of 55 and 59% resulted (Table 1, entries 2 and 3). When toluene was used as the solvent, the yield of **4a** was improved to 74% (Table 1, entry 4). The replacement of the isopropyl group in the quinoline *N*-oxide with an ethyl group led to another efficient oxidant (Table 1, entry 5). However, sterically less demanding 8-methylquinoline *N*-oxide (**3c**) was less effective and provided **4a** in 56% yield (Table 1, entry 6). Subsequent catalyst screening revealed that [PPh_3Au]NTf_2 exhibited the best catalytic performance (Table 1, entry 9). The addition of 4 Å molecular sieves to the reaction mixture led to a further increase in the yield of **4a** to 88% (Table 1, entry 10). Pyridine *N*-oxide and 3,5-dichloropyridine *N*-oxide also acted as oxidants to afford **4a** in 76 and 42% yield, respectively (Table 1, entries 13 and 14). In most cases, we observed the formation of a small amount of the 1,3-diketone **5**, which results from a competitive 1,2-H shift of the gold carbenoid intermediate.

For example, from the reaction described in Table 1, entry 10, compound **5**, which exists as keto/enol tautomers according to NMR spectroscopy, was isolated in 10% yield. The oxidation of **1a** occurred regioselectively at the alkyne position substituted with the phenyl group. [PPh_3AuCl] or $AgNTf_2$ were ineffective as catalysts for the production of **4a** (Table 1, entries 15 and 16). The γ-carboline skeleton has been identified as a superior scaffold structure in many biologically active compounds.[11] However, there is no general efficient route for the synthesis of highly functionalized γ-carbolines,[12] especially those that contain substituents in the 1- and 4-positions.[13] Our method provides a straightforward route to these heterocycles.

We next explored the scope of this gold-catalyzed oxidative cycloaddition/rearrangement reaction under the optimized condtions, first with respect to the α-indolyl-substituted propargylic alcohol substrate. A wide range of secondary propargylic alcohols were converted into the desired γ-carbolines within a short reaction period (2 h; Scheme 3). Substrates with aryl groups on the alkyne terminus underwent the cyclization reaction smoothly, regardless of the electronic nature of the substituent on the

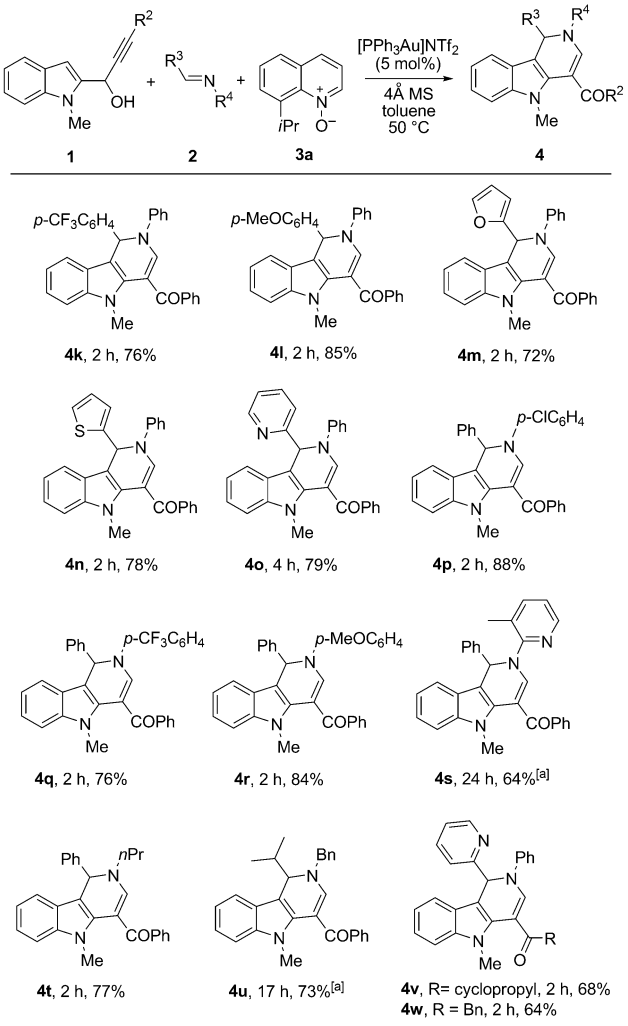


Scheme 3. Scope of the reaction with respect to the propargylic alcohol (**1**/**2a**/**3a** 1.3 : 1 : 1.4). The yields given are for the isolated product. [a] The reaction was carried out with catalyst **A** (5 mol%) and 4 Å MS in DCE at 50 °C for 2 h. Bn = benzyl.

aromatic ring (*p*-CF_3, *p*-MeO), to give **4b** and **4c** in similar yields of 75 and 74%, respectively. A thienyl group was also compatible with this reaction, with the formation of **4d** in 80% yield. A cyclohexenyl-substituted alkyne was also converted into the corresponding product **4e** in good yield

(79%). The reactions of alkynes with an alkyl, such as propyl or cyclopropyl, or benzyl substituent were also satisfactory, and led to **4f–h** in 51–74% yield. As for the indole moiety, an *N*-benzyl-protected indole as well as a nonprotected indole were both found to be suitable for this reaction: products **4i** and **4j** were obtained in 63 and 53% yield, respectively.

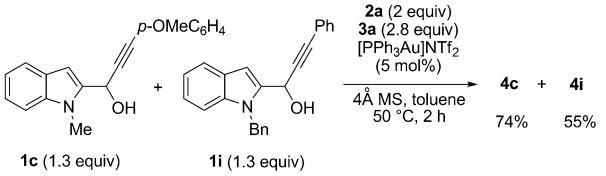
The scope of the reaction with respect to the imine component was also examined with **1a** as a reaction partner in most cases (Scheme 4). The reactions of *C*-(*p*-trifluoromethylphenyl) and *C*-(*p*-methoxyphenyl)-substituted imines with **1a** proceeded well to furnish **4k** and **4l** in 76 and 85%



Scheme 4. Scope of the reaction with respect to the imine substrate (**1**/**2**/**3a** 1.3 : 1 : 1.4). The yields given are for the isolated product. [a] $[PPh_3Au]NTf_2$ (10 mol%) was used.

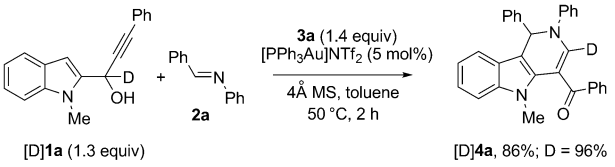
yield, respectively. The results indicated that the electronic nature of the *C*-aryl ring had little influence on the product yield. Furanyl-, thienyl-, and 2-pyridyl-substituted imines were also tolerated well and reacted with **1a** to give **4m–o** in 72–79% yield. Imines with *N*-aryl groups bearing *p*-Cl, *p*-CF_3, and *p*-MeO substituents reacted smoothly with **1a** to afford **4p–r** in 76–88% yield. A reaction with the more sterically encumbered *N*-2-(3-methylpyridyl)-substituted imine provided **4s** in 64% yield after 24 h. The N substituent can also be aliphatic. For example, an *N*-propyl imine underwent cyclization efficiently to afford **4t** in 77% yield. An imine bearing alkyl groups at both ends of the C=N bond also participated in this cycloaddition reaction, albeit with a longer reaction time (product **4u**). Substrates **1** bearing alkyl substituents reacted well with different imines. Thus, compounds **4v** and **4w** were produced in 68 and 64% yield, respectively, in a reaction with a *C*-(2-pyridyl)-substituted imine.

To gain an understanding of the acyl-migration process, we performed a cross-over experiment. The subjection of a mixture of two different propargylic alcohols, **1c** and **1i**, to the catalytic reactions conditions provided **4c** and **4i** in 74 and 55% yield, respectively (Scheme 5). No cross-over product was observed by LC–MS analysis of the crude reaction mixture. The result indicated that acyl migration occurred intramolecularly.



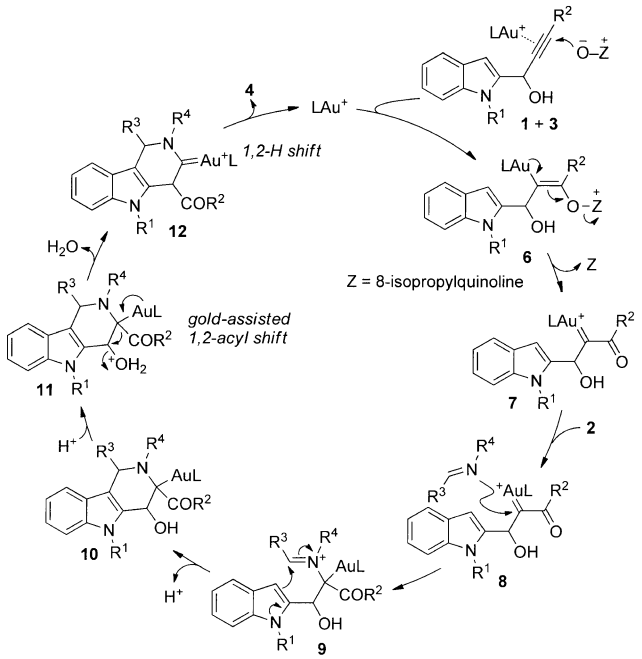
Scheme 5. Cross-over experiment.

We also prepared the deuterium-labeled propargylic alcohol [D]**1a** to probe the reaction mechanism. The treatment of [D]**1a** with **2a** under the standard reaction conditions in the presence of the gold catalyst provided [D]**4a** in 86% yield without significant loss of deuterium (Scheme 6). This result indicated that a concerted 1,2-H shift occurred during the reaction process.



Scheme 6. Deuterium-labeling experiment.

A mechanistic proposal for the formation of dihydro-γ-carbolines **4** is depicted in Scheme 7. Initially, highly regioselective nucleophilic attack of the quinoline *N*-oxide on the gold-activated alkyne, followed by fragmentation, leads to an α-carbonyl gold carbenoid **7**. The regioselectivity is consistent with that reported by Hashmi et al. for the gold-catalyzed oxidative rearrangement of propargylic alcohols to 1,3-diketones.[3n] They also suggested that gold carbenoid species might be formed by the *syn* addition of a gold *N*-oxide complex to the alkyne, followed by fragmentation.[3n] Subsequent nucleophilic attack of the imine nitrogen atom on the highly electrophilic gold carbenoid **7** generates an iminium intermediate **9**. Alternatively, **9** might also be formed by



Scheme 7. Possible reaction mechanism.

direct addition of the imine to the vinyl gold species **6**. Next, intramolecular nucleophilic addition of the indolyl moiety to the iminium ion in **9** delivers an alkyl gold intermediate **10**. This step is followed by gold-assisted 1,2-acyl migration[14,15] and a subsequent 1,2-H shift to furnish the final product **4**.[16] The formation of a gold carbenoid **12** or gold-stabilized carbocation might serve as a driving force for this rearrangement. Intermediate **12** might also be stabilized by the nitrogen atom adjacent to the gold carbenoid. Lewis acid catalyzed 1,2-carbonyl migrations in pinacol-type rearrangements have been observed for chlorohydrins,[17] α,β-epoxyketones,[18] and esters;[19] for these processes, a concerted mechanism involving neighboring-group participation by the carbonyl group was suggested.[18d]

In summary, we have developed a gold-catalyzed synthesis of highly functionalized dihydro-γ-carbolines by the cyclization of α-(2-indolyl) propargylic alcohols with imines in the presence of 8-isopropylquinoline *N*-oxide as the oxidant. This method offers several advantages, such as mild reaction conditions, high regioselectivity, and readily accessible starting materials. The reaction most likely proceeds through the intermolecular trapping of an α-carbonyl gold carbenoid intermediate by the imine, followed by cyclization and a novel gold-assisted 1,2-acyl migration, and is one of the few examples of a gold-catalyzed intermolecular annulation reaction involving α-carbonyl gold carbenoid species. Clarification of the reaction mechanism and further application of this chemistry are in progress.[20]

Experimental Section

General procedure: An α-(2-indolyl) propargylic alcohol **1** (0.26 mmol), an imine **2** (0.2 mmol), 8-isopropylquinoline *N*-oxide (**3a**; 52.4 mg, 0.28 mmol), toluene (2 mL), 4 Å MS (50 mg), and $[PPh_3Au]NTf_2$ (7.4 mg, 0.01 mmol) were added successively to a Schlenk tube at room temperature. The resulting solution was stirred at 50 °C until the reaction was complete, as monitored by thin-layer chromatography. The reaction mixture was quenched with two drops of Et_3N. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel to afford the desired dihydro-γ-carboline product **4**.

Received: May 31, 2013
Revised: July 24, 2013
Published online: September 3, 2013

Keywords: 1,2-acyl migration · dihydro-γ-carbolines · gold · homogeneous catalysis · propargylic alcohols

[1] For reviews on gold-catalyzed oxidative reactions of alkynes, see: a) J. Xiao, X. W. Li, *Angew. Chem.* **2011**, *123*, 7364; *Angew. Chem. Int. Ed.* **2011**, *50*, 7226; b) M. Rudolph, A. S. K. Hashmi, *Chem. Soc. Rev.* **2012**, *41*, 2448; c) N. D. Shapiro, F. D. Toste, *Synlett* **2010**, 675; for reviews on gold-catalyzed reactions, see: d) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180; e) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410; f) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351; g) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326; h) N. T. Patil, Y. Yamamoto, *Chem. Rev.* **2008**, *108*, 3395; i) S. M. Abu Sohel, R.-S. Liu, *Chem. Soc. Rev.* **2009**, *38*, 2269; j) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208; k) A. S. K. Hashmi, M. Bührle, *Aldrichimica Acta* **2010**, *43*, 27; l) A. S. Dudnik, N. Chernyak, V. Gevorgyan, *Aldrichimica Acta* **2010**, *43*, 37; m) M. Bandini, *Chem. Soc. Rev.* **2011**, *40*, 1358; n) N. T. Patil, *Chem. Asian J.* **2012**, *7*, 2186.

[2] For reactions with diphenyl sulfoxide as the oxidant, see: a) C. A. Witham, P. Mauleón, N. D. Shapiro, B. D. Sherry, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 5838; b) G. Li, L. Zhang, *Angew. Chem.* **2007**, *119*, 5248; *Angew. Chem. Int. Ed.* **2007**, *46*, 5156; c) C.-W. Li, K. Pati, G.-Y. Lin, S. M. A. Sohel, H.-H. Hung, R.-S. Liu, *Angew. Chem.* **2010**, *122*, 10087; *Angew. Chem. Int. Ed.* **2010**, *49*, 9891; d) A. B. Cuenca, S. Montserrat, K. M. Hossain, G. Mancha, A. Lledos, M. Medio-Simon, G. Ujaque, G. Asensio, *Org. Lett.* **2009**, *11*, 4906; e) C.-F. Xu, M. Xu, Y.-X. Jia, C.-Y. Li, *Org. Lett.* **2011**, *13*, 1556.

[3] For reactions with quinoline/pyridine *N*-oxide as the oxidant, see: a) L. Ye, L. Cui, G. Zhang, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 3258; b) L. Ye, W. He, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 8550; c) B. Lu, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 14070; d) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das, R.-S. Liu, *Angew. Chem.* **2011**, *123*, 7043; *Angew. Chem. Int. Ed.* **2011**, *50*, 6911; e) P. W. Davies, A. Cremonesi, N. Martin, *Chem. Commun.* **2011**, *47*, 379; f) D. Qian, J. Zhang, *Chem. Commun.* **2011**, *47*, 11152; g) Y. Luo, G. Zhang, E. S. Hwang, T. A. Wilcoxon, L. Zhang, *Beilstein J. Org. Chem.* **2011**, *7*, 596; h) L. Ye, Y. Wang, D. H. Aue, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 31; i) E. L. Noey, Y. Luo, L. Zhang, K. N. Houk, *J. Am. Chem. Soc.* **2012**, *134*, 1078; j) Y. Wang, K. Ji, S. Lan, L. Zhang, *Angew. Chem.* **2012**, *124*, 1951; *Angew. Chem. Int. Ed.* **2012**, *51*, 1915; k) S. Bhunia, S. Ghorpade, D. B. Huple, R.-S. Liu, *Angew. Chem.* **2012**, *124*, 2993; *Angew. Chem. Int. Ed.* **2012**, *51*, 2939; l) M. Murai, S. Kitabata, K. Okamoto, K. Ohe, *Chem. Commum.* **2012**, *48*, 7622; m) W. Yuan, X. Dong, Y. Wei, M. Shi, *Chem. Eur. J.* **2012**, *18*, 10501; n) A. S. K. Hashmi, T. Wang, S. Shi, M. Rudolph, *J. Org. Chem.* **2012**, *77*, 7761; o) W. He, L. Xie, Y. Xu, J. Xiang, L. Zhang, *Org. Biomol. Chem.* **2012**, *10*, 3168.

[4] For reactions with nitrones as the oxidant, see: a) H.-S. Yeom, J.-E. Lee, S. Shin, *Angew. Chem.* **2008**, *120*, 7148; *Angew. Chem. Int. Ed.* **2008**, *47*, 7040; b) H.-S. Yeom, Y. Lee, J. Jeong, E. So, S.

Hwang, J.-E. Lee, S. S. Lee, S. Shin, *Angew. Chem.* **2010**, *122*, 1655; *Angew. Chem. Int. Ed.* **2010**, *49*, 1611; c) D. Chen, G. Song, A. Jia, X. Li, *J. Org. Chem.* **2011**, *76*, 8488.

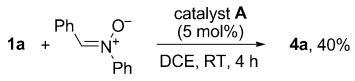
[5] W. He, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 8482.

[6] a) Y. Luo, K. Ji, Y. Li, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 17412; b) recently, an efficient intermolecular trapping of α-oxo gold carbenes with carboxylic acids was also reported by the Zhang research group: K. Ji, Y. Zhao, L. Zhang, *Angew. Chem.* **2013**, *125*, 6636; *Angew. Chem. Int. Ed.* **2013**, *52*, 6508.

[7] A. Mukherjee, R. B. Dateer, R. Chaudhuri, S. Bhunia, S. N. Karad, R.-S. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 15372.

[8] a) Y. Lu, X. Du, X. Jia, Y. Liu, *Adv. Synth. Catal.* **2009**, *351*, 1517; b) G. Li, Y. Liu, *J. Org. Chem.* **2010**, *75*, 3526; c) L. Wang, G. Li, Y. Liu, *Org. Lett.* **2011**, *13*, 3786; d) X. Xie, X. Du, Y. Chen, Y. Liu, *J. Org. Chem.* **2011**, *76*, 9175.

[9] We envisioned that a nitrone might also oxidize propargyl alcohols **1** to generate a gold carbenoid intermediate that would be trapped by the released imine to form the same product **4**. Indeed, the reaction occurred as expected; however, the highest yield of **4a** observed so far was 40%.



[10] CCDC 938876 (**4c**), 938877 (**4e**), 938875 (**4k**), 938879 (**4v**), and 938878 (**4w**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[11] a) J. Chen, T. Liu, R. Wu, J. Lou, X. Dong, Q. He, B. Yang, Y. Hu, *Eur. J. Med. Chem.* **2011**, *46*, 1343; b) M. T. A. Salim, Y. Goto, T. Hamasaki, M. Okamoto, H. Aoyama, Y. Hashimoto, S. Musiu, J. Paeshuyse, J. Neyts, M. Froeyen, P. Herdewijn, M. Baba, *Antiviral Res.* **2010**, *88*, 263; c) A. Bridoux, R. Millet, J. Pommery, N. Pommery, J. Henichart, *Bioorg. Med. Chem.* **2010**, *18*, 3910; d) A. V. Ivachtchenko, E. B. Frolov, O. D. Mitkin, V. M. Kysil, A. V. Khvat, I. M. Okun, S. E. Tkachenko, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3183; e) J. Bonjoch, F. Diaba, L. Pagès, D. Pérez, L. Soca, M. Miralpeix, D. Vilella, P. Anton, C. Puig, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4299; f) K. Sako, H. Aoyama, S. Sato, Y. Hashimoto, M. Baba, *Bioorg. Med. Chem.* **2008**, *16*, 3780; g) N. Khorana, A. Purohit, K. Herrick-Davis, M. Teitler, R. A. Glennon, *Bioorg. Med. Chem.* **2003**, *11*, 717; h) N. Khorana, C. Smith, K. Herrick-Davis, A. Purohit, M. Teitler, B. Grella, M. Dukat, R. A. Glennon, *J. Med. Chem.* **2003**, *46*, 3930; i) M. Abou-Gharbia, U. R. Patel, M. B. Webb, J. A. Moyer, T. H. Andree, E. A. Muth, *J. Med. Chem.* **1987**, *30*, 1818.

[12] For the synthesis of γ-carbolines, see: a) H. Zhang, R. C. Larock, *Org. Lett.* **2001**, *3*, 3083; b) H. Zhang, R. C. Larock, *J. Org. Chem.* **2002**, *67*, 7048; c) S. Chiba, Y.-J. Xu, Y.-F. Wang, *J. Am. Chem. Soc.* **2009**, *131*, 12886; d) S. Ding, Z. Shi, N. Jiao, *Org. Lett.* **2010**, *12*, 1540; e) H. Dong, R. T. Latka, T. G. Driver, *Org. Lett.* **2011**, *13*, 2726.

[13] J. H. Wynne, W. M. Stalick, *J. Org. Chem.* **2003**, *68*, 4845.

[14] Recently, a gold-catalyzed cycloisomerization involving a pinacol-type 1,2-acyl migration was reported: Y. Xiong, S. E. Schaus, J. A. Porco, Jr, *Org. Lett.* **2013**, *15*, 1962.

[15] For a platinum-catalyzed ring expansion of methylenecyclopropane involving 1,2-alkyl migration, see: A. Fürstner, C. Aïssa, *J. Am. Chem. Soc.* **2006**, *128*, 6306.

[16] As suggested by a reviewer, we also prepared enantiomerically pure **1a** by optical resolution through HPLC on a chiral phase to probe a possible chirality transfer; however, the results indicated that chirality transfer does not occur under the standard reaction conditions.

[17] J. M. Domagala, R. D. Bach, *J. Am. Chem. Soc.* **1979**, *101*, 3118.

[18] a) H. O. House, *J. Am. Chem. Soc.* **1954**, *76*, 1235; b) H. O. House, G. D. Ryerson, *J. Am. Chem. Soc.* **1961**, *83*, 979; c) J. M. Domagala, R. D. Bach, *J. Am. Chem. Soc.* **1978**, *100*, 1605; d) R. D. Bach, J. M. Domagala, *J. Org. Chem.* **1984**, *49*, 4181.

[19] J. M. Domagala, R. D. Bach, J. Wemple, *J. Am. Chem. Soc.* **1976**, *98*, 1975.

[20] **Addendum**: The reaction might also proceed through 1,2-indolyl migration of a gold carbenoid **7** followed by [4+2] cycloaddition with imine. We thank Prof. Liming Zhang for this valuable suggestion.

