

Gold(I)-Catalyzed Oxidative Cleavage of a C–C Double Bond in Water

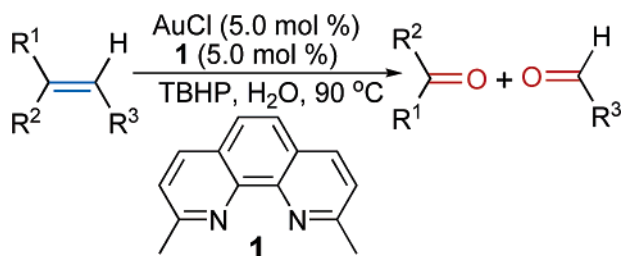
Dong Xing,[†] Bingtao Guan,[‡] Guixin Cai,[‡] Zhao Fang,[‡] Liping Yang,[†] and Zhangjie Shi^{*†}

Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China, State Key Laboratory of Organometallic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China, and Department of Chemistry, East China Normal University, Shanghai 200062, China

zshi@pku.edu.cn

Received November 23, 2005

ABSTRACT



Oxidative cleavage of the C=C bond to afford ketone or aldehyde products with *tert*-butyl hydrogenperoxide (TBHP) as the oxidant can be catalyzed by AuCl with neocuproine (1) in water.

Organic transformations catalyzed by gold complexes have been a focus of attention in recent years.¹ New transformations, such as direct arene functionalizations² and carbene insertions to benzene, O–H, and N–H bonds,³ have been developed. Both gold(I) and gold(III) species also showed unique activities in mediating reactions involving alkynes and alkenes.⁴ In contrast, gold-catalyzed oxidation chemistry, in particular oxygen transfer reactions, has been less developed, which should have potential applications in synthetic

oxidation chemistry. So far, only oxidation of carbon monoxide and alcohols mediated by heterogeneous gold nanoparticles were reported.⁵ The homogeneous oxidation chemistry catalyzed by gold is still limited.⁶ Herein, we report

[†] East China Normal University.

[‡] Peking University.

(1) (a) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51–65. (b) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387–391. (c) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164–11165. (d) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978–15979. (e) Wei, C.; Li, C.-J. *J. Am. Chem. Soc.* **2003**, *125*, 9584–9585. (f) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806–11807. (g) Yao, X.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 6884–6885. (h) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402–2406. (i) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415–1418. (j) Arcadi, A.; Giuseppe, S. D.; Marinelli, F.; Rossi, E. *Adv. Synth. Catal.* **2001**, *343*, 443–446. (k) Hashmi, A. S. K.; Ding, L.; Bats, J. W.; Fischer, P.; Frey, W. *Chem.–Eur. J.* **2003**, *9*, 4339–4345. and references therein.

(2) (a) Nevado, C.; Echavarren, A. M. *Synthesis* **2005**, *2*, 167–182. (b) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650–12651. (c) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596–13597. (d) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669–3671. (e) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 5964–5965. (f) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285–2288. (g) Dyker, G.; Muth, E.; Hashmi, A. S. K.; Ding, L. *Adv. Synth. Catal.* **2003**, *345*, 1247–1252. (h) Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485–3496. (i) Alfonsi, M.; Arcadi, A.; Aschi, M.; Bianchi, G.; Marinelli, F. *J. Org. Chem.* **2005**, *70*, 2265–2273. (j) Nevado, C.; Echavarren, A. M. *Chem.–Eur. J.* **2005**, *11*, 3155–3164.

(3) Fructos, M. R.; Belderrain, T. R.; de Frémont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. *J. Angew. Chem., Int. Ed.* **2005**, *44*, 5284–5288.

(4) (a) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802–5803. (b) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962–6963. (c) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654–8655. (d) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858–10859. (e) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, *127*, 6966–6967.

a unique process of oxidizing the C=C bond to afford ketone or aldehyde products with tertiary butyl hydrogenperoxide (TBHP) as the oxidant in water.

Olefins are important building blocks in organic synthesis and are utilized broadly as starting materials to construct complex structures with methods such as the Wacker process, epoxidation, etc.⁷ The cleavage of the C=C bond to form two carbonyl products is a synthetically useful method, which is usually achieved by ozonation followed by reduction or by dihydroxylation followed by oxidation.⁸ We chose 1,1-diphenylethylene (**2a**) as the starting substrate to explore new gold-catalyzed oxidation of olefins because conjugation to the phenyl groups activates the olefin.⁹ We first tested the reaction with TBHP as the oxidant and AuCl as the catalyst in the absence of any ligand in toluene. Only a small amount of benzophenone was produced (entry 3, Table 1). Then, we chose to investigate gold complexes supported by various ligands.^{3,5,10,11} It has been shown that the linear or four-coordinated gold(I) complexes can be prepared with support of different bidentate nitrogen ligands.¹² We tested the reactions with different nitrogen-based ligands such as pyridine, bipyridine, and phenanthroline. These did not provide good conversions to the reactions. To our delight, with the use of neocuprione (**1**) as the ligand, the oxidation of **2a** ran efficiently to produce benzophenone **3a** as the product in 90% isolated yield in toluene (entry 4, Table 1). When AgOTf was used to remove the chloride from AuCl,^{3b,5g,13} the efficiency of oxidation only increased slightly

Table 1. Oxidative Cleavage of Diphenyl Ethylene

Reaction scheme: Diphenyl ethylene (**2a**) reacts with TBHP (2.5 equiv) in a solvent at 90 °C, catalyzed by AuCl (5.0 mol %) and ligand **L** (5.0 mol %), to produce benzophenone (**3a**).

| entry | catalyst | L | solvent | time (h) | yield ^a (%) |
|-----------------|-------------------|----------------|------------------|----------|------------------------|
| 1 ^b | | | toluene | 10 | <5 |
| 2 ^b | | 1 | toluene | 10 | <5 |
| 3 ^b | AuCl | | toluene | 10 | <5 |
| 4 | AuCl | 1 | toluene | 10 | 90 |
| 5 ^c | AuCl | 1 | toluene | 10 | 92 |
| 6 ^b | AuCl ₃ | 1 | toluene | 10 | <20 |
| 7 ^b | AuCl | 1 | toluene | 10 | <5 |
| 8 ^b | AuCl | 1 | EtOH | 10 | <5 |
| 9 ^b | AuCl | 1 | MeCN | 10 | <5 |
| 10 ^b | AuCl | 1 | THF | 10 | <5 |
| 11 ^b | | 1 | H ₂ O | 24 | <10 |
| 12 ^b | AuCl | | H ₂ O | 24 | <10 |
| 13 | AuCl | py | H ₂ O | 10 | 41 |
| 14 | AuCl | bipy | H ₂ O | 10 | 23 |
| 15 | AuCl | phenanthroline | H ₂ O | 10 | 16 |
| 16 | AuCl | 1 | H ₂ O | 2 | 93 |
| 17 ^b | AuCl ₃ | 1 | H ₂ O | 2 | <10 |
| 18 ^d | AuCl | 1 | H ₂ O | 6 | 92 |

^a Isolated yield. ^b GC yield with the use of decane as an internal standard. ^c 5.0 mol % of AgOTf was used as the cocatalyst. ^d 1.0 mol % of AuCl and 1.0 mol % of **1** were used as the catalyst.

(5) (a) Abad, A.; Concepción, P.; Corma, A.; García, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 4066–4069. (b) Kim, W. B.; Voitl, T.; Rodriguez-Rivera, G. J.; Dumesic, J. A. *Science* **2004**, *305*, 1280–1283. (c) Biella, S.; Castiglioni, G. L.; Fumagalli, C.; Prati, L.; Rossi, M. *Catal. Today* **2002**, *72*, 43–49 and references therein.

(6) (a) Boring, E.; Geletti, Y. V.; Hill, C. L. *J. Am. Chem. Soc.* **2001**, *123*, 1625. (b) Guan, B.; Xing, D.; Cai, G.; Wan, X.; Yu, N.; Fang, Z.; Yang, L.; Shi, Z. *J. Am. Chem. Soc.* **2005**, *127*, 18004–18005. (c) Cinellu, M. A.; Minghetti, G.; Cocco, F.; Stoccoro, S.; Zucca, A.; Manassero, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6892–6895.

(7) (a) Gasparri, F.; Giovannoli, M.; Misiti, D.; Natile, G.; Palmieri, G. *J. Org. Chem.* **1990**, *55*, 1323–1328. (b) Baeyer, A.; Villiger, V. *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3625–3633.

(8) (a) McReynolds, D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239–2258. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285–2310 and references therein.

(9) (a) Molander, M. G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236–8246. (b) Yu, W.; Mei, Y.; Kang, Y.; Hua, Z.; Jin, Z. *Org. Lett.* **2004**, *6*, 3217–3219.

(10) (a) Döbler, C.; Mehlretter, G. M.; Sundermeier, U.; Beller, M. *J. Am. Chem. Soc.* **2000**, *122*, 10289–10297. (b) Adam, W.; Mock-Knoblach, C.; Saha-Möeller, C. R.; Herderich, M. *J. Am. Chem. Soc.* **2000**, *122*, 9685–9691. (c) Rodriguez, A. L.; Bunlaksanusorn, T.; Knochel, P. *Org. Lett.* **2000**, *2*, 3285–3287. (d) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 9546–9547. (e) Dai, M. J.; Wang, C. H.; Dong, G. B.; Xing, J.; Luo, T. P.; Liang, B.; Chen, J. H.; Yang, Z. *Eur. J. Org. Chem.* **2003**, 4346–4348.

(11) (a) Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejović, E. *Angew. Chem., Int. Ed.* **2004**, *43*, 6545–6547. (b) Hashmi, A. S. K.; Rudolph, M.; Weyrauch, J. P.; Wölflle, M.; Frey, W.; Bats, J. W. *Angew. Chem., Int. Ed.* **2005**, *44*, 2798–2801.

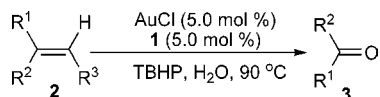
(12) (a) Dávila, R. M.; Staples, R. J.; Fackler, J. P. *Organometallics* **1994**, *13*, 418–420. (b) Cinellu, M. A.; Minghetti, G.; Stoccoro, S.; Zucca, A.; Manassero, M. *Chem. Commun.* **2004**, 1618–1619. (c) Vicente, J.; Chicote, M.-T.; Guerrero, R.; Jones, P. G.; Ramírez de Arellano, M. C. *Inorg. Chem.* **1997**, *36*, 4438–4443. (d) Yamamoto, Y.; Shiotsuka, M.; Okuno, S.; Onaka, S. *Chem. Lett.* **2004**, *33*, 210–211. (e) Vicente, J.; Arcas, A.; Jones, P. G.; Lautner, J. J. *Chem. Soc., Dalton Trans.; Inorg. Chem.* **1990**, 451–456.

(13) (a) Markham, J. P.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 9708–9709. (b) Muñoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M. *Organometallics* **2005**, *24*, 1293–1300.

(entry 5, Table 1). The oxidation reactions were also studied in other common organic solvents, such as acetone, THF, EtOH, and MeCN; however, the conversions and yields were much lower than those in toluene (entries 7–10, Table 1). Remarkably, we discovered that this reaction can run efficiently in water. Product **3a** was isolated in 93% yield with 5 mol % of AuCl plus ligand **1** (entry 16, Table 1). Similarly, the reactions did not proceed when other ligands, such as pyridine, bipyridine, and phenanthroline, were employed in water (entries 13–15, Table 1). Furthermore, only a small amount of **3a** was generated with either AuCl or **1** as the catalyst under the same conditions (entries 11 and 12, Table 1). The catalyst loading could be decreased to 1.0 mol %, and the reaction still ran smoothly to afford **3a** in high isolated yield when a longer reaction time was used (entry 18, Table 1). To exclude the gold(III) species as a potential catalyst under such an oxidizing condition, AuCl₃ was employed to replace AuCl. This reaction produced a mixture with only a small amount of ketone product, which can be detected by GC, and most of the starting material was recovered (entries 6 and 17, Table 1).

A range of substrates were investigated as listed in Table 2. We found, with the use of substituted geminal biaryl ethylenes as substrates, that the reactions ran quite smoothly, and corresponding products were produced in moderate to excellent yields. With either electron-donating or electron-withdrawing groups at the para position of one of the phenyl rings, oxidative reactions ran efficiently and finished in 3–6 h (entries 2–3 and 6–7, Table 2). The reaction was slowed

Table 2. Oxidative Cleavage of Substituted Styrenes to Ketones and Aldehydes^{a,b}



| entry | R ¹ | R ² | R ³ | time (h) | 3 (%) |
|------------------|---|---|-----------------|----------|----------------|
| 1 ^{c,d} | C ₆ H ₅ | C ₆ H ₅ | H | 3 | 3a (93) |
| 2 | C ₆ H ₅ | 4-CH ₃ C ₆ H ₄ | H | 3 | 3b (84) |
| 3 | C ₆ H ₅ | 4-CH ₃ OC ₆ H ₄ | H | 3 | 3c (70) |
| 4 | C ₆ H ₅ | 2-CH ₃ C ₆ H ₄ | H | 18 | 3d (89) |
| 5 | C ₆ H ₅ | 1-C ₁₀ H ₇ | H | 24 | 3e (56) |
| 6 | C ₆ H ₅ | 4-FC ₆ H ₄ | H | 3 | 3f (62) |
| 7 | C ₆ H ₅ | 4-BrC ₆ H ₄ | H | 6 | 3g (86) |
| 8 | C ₆ H ₅ | 2-CH ₃ O-5-ClC ₆ H ₃ | H | 3 | 3h (44) |
| 9 | C ₆ H ₅ | 2-thiophenyl | H | 24 | 3i (53) |
| 10 | C ₆ H ₅ | CH ₃ | H | 36 | 3j (39) |
| 11 | C ₆ H ₅ | H | CH ₃ | 36 | 3k (66) |
| 12 | C ₆ H ₅ | H | H | 36 | 3k (56) |
| 13 | 4-AcOCH ₂ C ₆ H ₄ | H | H | 24 | 3l (62) |
| 14 | 2-C ₁₀ H ₇ | H | H | 24 | 3m (52) |
| 15 ^e | 4-CH ₃ O ₂ CC ₆ H ₄ | H | H | 36 | 3n (20) |

^a Isolated yield. ^b Small molecules, such as formaldehyde, were not detected in these reactions. ^c 1.0 mol % of AuCl and 1.0 mol % of **1** were used as the catalyst. ^d Phenyl hydrazine was used to trap formaldehyde, and 2-methylene-1-phenylhydrazine was isolated as a product in 30% yield. ^e 68% of starting material was recovered.

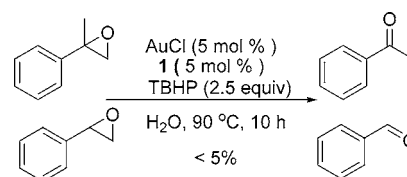
with substrates bearing substituted groups at the ortho position of the phenyl groups, such as 2-toluy and 1-naphthyl (entries 4 and 5, Table 2). These results indicated that the electronic effect on the phenyl group in these geminal diaryl ethylenes did not play a significant role in affecting the rate of oxidation, probably because of the high reactivity of these substrates. In contrast, steric hindrance seems to be a key factor in affecting the rate of oxidation of these substrates.

Moreover, various functional groups, such as alkyl, alkoxy, and halide groups on phenyl rings, were well tolerated under this condition (entries 2–8, Table 2). With the methyl group at the benzyl position in the geminal diaryl alkenes, potential byproducts from the radical oxidation of the methyl group were not observed (entries 2 and 4, Table 2). A heterocyclic substrate could be employed, and the corresponding product was obtained in a moderate yield (entry 9, Table 2). Oxidation of α -methyl styrene was carried out, and acetophenone was acquired in 39% isolated yield (entry 10, Table 2). Subsequently, β -styrene can also be oxidized to afford benzaldehyde in 66% isolated yield (entry 11, Table 2). With these two substrates, the competing radical oxidation of the allylic methyl groups was observed to give the aldehydes as byproducts in 31% and 16% isolated yields, respectively, together with lower yields of the desired carbonyl products (entries 10 and 11, Table 2).

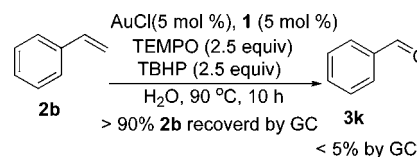
Finally, styrene and 2-vinylnaphthylene were studied under this condition and the corresponding aldehydes were obtained with 5.0 mol % of AuCl and **1** as the catalyst in moderate isolated yields (entries 12–14, Table 2). The ester as a substituted group at the benzylic position could survive this

reaction (entry 13, Table 2). However, because the efficiency of the oxidation decreased because of the presence of an electron-withdrawing group on the phenyl ring with methyl *p*-vinylbenzoate as a starting material, the aldehyde was isolated from this reaction in only 20% yield with 68% of the starting material recovered (entry 15, Table 2). During this process, the byproduct formaldehyde was detected by trapping the reaction mixture with phenyl hydrazine. 2-Methylene-1-phenylhydrazine was isolated as a product in 30% yield (entry 1, Table 2). This result strongly indicated that the C=C bond was split into two carbonyl products in the reaction. It should be noted that the over-oxidation to acid was not observed under these conditions. Oxidation of styrenes to give aldehydes and ketones has been studied in the past.¹⁴ The new gold-catalyzed process we report here is efficient, simple, and can tolerate various functional groups.

Mechanistically, this reaction may proceed in two steps involving the first step of epoxidation¹⁵ and a subsequent oxidation to produce carbonyl products.¹⁶ To test this mechanism, the reactions were carried out with two epoxides, 2-methyl-2-phenyloxirane and styrene oxide, which were prepared from α -methyl styrene and styrene, respectively.¹⁷ However, no carbonyl products were observed in either reaction (eq 1). Thus, the mechanism involving epoxides as



the intermediates could be excluded. Our study also indicated that (Neo)AuCl and [(Neo)Au(styrene)]⁺ could be observed by ESI mass spectroscopy in the catalytic cycle. Many mechanistic possibilities should be considered. It seems to us that the interaction of olefin to a gold center to give the complexes such as [(Neo)Au(styrene)]⁺ may be important. The bulky groups and the electron-withdrawing substitutions might affect the rate of oxidation because of their varied binding affinities to gold(I). We also found that this oxidation was completely inhibited by TEMPO (eq 2),¹⁸ which may suggest a radical initiation pathway; however, the benzylic methyl group survived well under this condition.



In summary, we developed a novel method to oxidize olefins to form ketones or aldehydes with the use of a gold-

(14) (a) Clennan, E. L.; Pan, G.-L. *Org. Lett.* **2003**, *5*, 4979–4982. (b) Barton, D. H. R.; Wang, T.-L. *Tetrahedron Lett.* **1994**, *35*, 1519–1522. (c) Adams, J. M.; Davies, S. E.; Graham, S. H.; Thomas, J. M. *Chem. Commun.* **1978**, 930–931. (d) Sarneski, J. E.; Michos, D.; Thorp, H. H.; Didiuk, M.; Poon, T.; Blewitt, J.; Brudvig, G. W.; Crabtree, R. H. *Tetrahedron Lett.* **1991**, *32*, 1153–1156.

(I) complex as the catalyst and TBHP as the oxidant. The novel redox activity of gold species was demonstrated. This oxidation reaction proceeds under mild conditions in water. A series of functional groups can be tolerated. This report could stimulate further research efforts on redox reactions, in particular oxygen transfers, mediated by gold species in solution. Further studies to probe the mechanism of these transformations, to unambiguously identify the catalytically

(15) Bhor, S.; Tse, M. K.; Klawonn, M.; Döbler, C.; Mägerlein, W.; Beller, M. *Adv. Synth. Catal.* **2004**, *346*, 263–267.

(16) Kurata, T.; Koshiyama, T.; Kawashima, H. *Yukagaku* **1987**, *36*, 206–209.

(17) Lane, B. S.; Burgess, K. *J. Am. Chem. Soc.* **2001**, *123*, 2933–2934.

(18) (a) Miller, J. B.; Salvador, J. R. *J. Org. Chem.* **2002**, *67*, 435–442.
(b) Hontis, L.; Vrindts, V.; Lutsen, L.; Vanderzande, D.; Gelan, J. *Polymer* **2001**, *42*, 5793–5796.

active species, and to broaden the scope of these reactions are currently ongoing and will be reported in due course.

Acknowledgment. Support of this work by a starter grant from Peking University and National Science Foundation of China (No. 20542001) is gratefully acknowledged. We are also indebted to Prof. Xi and Prof. Yang at Peking University for laboratory space and some chemicals for this research.

Supporting Information Available: Experimental procedures including compounds **3** along with spectroscopic and other data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL052830T