Tetrahedron 65 (2009) 1856–1858

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Gold-catalyzed benzylic oxidation to carbonyl compounds

Huanrong Li[a,*], Zhiping Li[a,*], Zhangjie Shi[b,c,*]

[a] Department of Chemistry, Renmin University of China, Beijing 100872, China
[b] Beijing National Laboratory of Molecular Sciences, Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry and Green Chemistry Center, Peking University, Beijing 100871, China
[c] State Key Laboratory of Organometallic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

ARTICLE INFO

Article history:
Received 30 June 2008
Received in revised form 2 December 2008
Accepted 2 December 2008
Available online 24 December 2008

ABSTRACT

The gold-catalyzed, mild and general benzylic oxidation toward carbonyl compounds with TBHP as oxidant is described. Corresponding products are obtained in moderate to excellent yields.

1. Introduction

Gold catalysis has rapidly become a hot topic in chemistry in the past decade. Gold species are equally effective as heterogeneous or homogeneous catalyst, which showed excellent results in diversified reactions.[1] Gold complexes have been employed as a highly efficient catalyst for the formation of C–C, C–O, C–N, C–S, and C–F bonds starting from alkenes and alkynes.[2] Recently great progress for direct functionalization of the C–H bond of electron-rich arenes to form new C–C bonds mediated by gold has been achieved.[3] However, research in homogeneous gold catalysis moved relatively slow for a long time. For example, gold was believed to be a rare element, but it is more abundant than palladium, platinum, rhodium, and many other precious metals. Gold compounds are easily reduced, but hard to oxidize due to the necessary change of oxidation states.[1a] This changed in 1987 when Haruta et al. reported the low-temperature selective oxidation of CO with O_2 catalyzed by solid-supported gold nanoparticles.[4] Also, many previous results showed that gold nanoparticles loaded on different solid supports showed unique reactivities in the oxidation of alcohol under basic conditions. However, the exact mechanism has not been clearly understood yet.[5] In contrast, selective oxidation via gold catalysis in homogeneous solution has rarely been reported. There is only one case in this field, which was given by Hill et al., who firstly found the oxidation of sulfide to sulfoxide with dioxygen catalyzed by gold(III) salt in aqueous solution.[6] Very recently, we and the other groups also showed that alcohols can be selectively oxidized to carbonyl compounds in toluene or in aqueous solution with dioxygen catalyzed by gold(I) complexes supported by bidentate N-donor ligands.[7,8] Obviously, the oxidation of alkene was also accomplished by gold complexes catalyzed oxygen transfer process. Herein we described the first general gold-catalyzed benzylic oxidation with *tert*-butyl hydroperoxide (**TBHP**).

2. Results and discussion

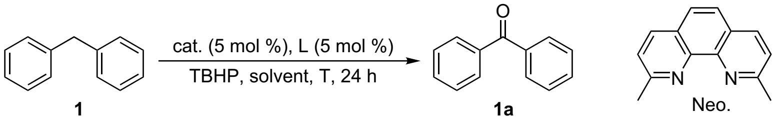
Our preliminary results showed that gold(I) complexes supported by neocuproine (Neo.) could catalyze the oxidative cleavage of C=C double bond to produce two carbonyl compounds when TBHP was used as the oxidant.[9] Interestingly, some alcohols could also be oxidized to carbonyl compounds under the same conditions with a 1:1 ratio of gold–Neo. In this study, our initial screening started from the direct oxidation of sp^3 C–H bonds. Diphenylmethane (**1a**) was chosen as a substrate for the optimization of the catalysis protocol. Generally, 5 mol % of catalyst was employed in our primary investigations with TBHP as the oxidant (Table 1). In the presence of 5 mol % of AuCl supported by Neo., different solvents, such as water and toluene were tested. Under these conditions, the product could be obtained in 39% yield (Table 1, entries 1 and 2). It seemed that the reaction was not sensitive to temperature since the results of the reaction didn't change significantly when the temperature was raised to 110 °C (Table 1, entry 3). Moreover, the product was isolated in only 46% yield even using 3 equiv of TBHP at 110 °C (Table 1, entry 4). $AuCl(PPh_3)$ or $KAuCl_4 \cdot 0.5H_2O$ in the presence of Neo. could also promote this oxidation, but the efficiency was very low (Table 1, entries 5–7). Absence of ligand made the efficiency of this reaction much lower (Table 1, entries 8 and 9). Other nitrogen ligands were investigated. The efficiency of oxidation was poor when TMEDA and pyridine were used as ligands in toluene (Table 1, entries 10 and 11). However, when the reaction was performed in pyridine for 10 h, the product was obtained in 84% yield (Table 1, entry 12). During this process, pyridine may play

---

* Corresponding authors.
E-mail addresses: hrli@ruc.edu.cn (H. Li), zhipingli@ruc.edu.cn (Z. Li), zshi@pku.edu.cn (Z. Shi).

0040-4020/$ – see front matter Crown Copyright © 2009 Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.12.055

Table 1
Oxidation of diphenylmethane with TBHP catalyzed by gold under different conditions[a]



Entry	Cat.	L	TBHP (equiv)	Solvents	T (°C)	**1a** (%)[b]
1	AuCl	Neo.	2	H_2O	90	39
2	AuCl	Neo.	2	Toluene	90	39
3	AuCl	Neo.	2	Toluene	110	44
4	AuCl	Neo.	3	Toluene	110	46
5	$AuCl(PPh_3)$	Neo.	2	Toluene	90	51
6	$KAuCl_4\cdot0.5H_2O$	Neo.	2	Toluene	90	57
7	$KAuCl_4\cdot0.5H_2O$	Neo.	2	H_2O	90	24
8	$KAuCl_4\cdot0.5H_2O$	—	2	H_2O	90	19
9	$KAuCl_4\cdot0.5H_2O$	—	2	Toluene	90	37
10	$KAuCl_4\cdot0.5H_2O$	TMEDA	2	Toluene	90	23
11	$KAuCl_4\cdot0.5H_2O$	Pyridine	2	Toluene	90	49
12[c]	$KAuCl_4\cdot0.5H_2O$	Pyridine	2	Pyridine	90	84
13	$KAuCl_4\cdot0.5H_2O$	Pyridine	2	Pyridine	90	99

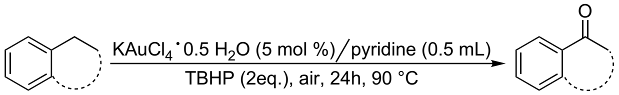
[a] All the reactions were carried out in the scale of 0.5 mmol of **1**.
[b] Isolated yields.
[c] The reaction was performed in pyridine for 10 h.

dual roles: ligand and solvent. We observed that the reaction could be completed to reach 99% yield if it took longer time (Table 1, entry 13).

Under the optimized reaction conditions, various diarylmethane substrates were subjected to oxidation (Table 2 and 3). Most diarylmethylene derivatives gave the corresponding products in excellent yields (up to >99%; Table 2, entries 1–6). Interestingly, the electronic effect of the substituents on aromatic ring of diarylmethylene derivatives was not observed. For example, the substrates bearing an electron-withdrawing group on the aromatic ring (Table 2, entries 3–5) produced products with 95–96% yields.

Less active substrates with one annelated aryl group in a cyclic system led to benzylic oxidation products with yields ranging between 57 and 65% (Table 3, entries 1–3). Dihydroisobenzofuran and tetrahydroisobenzopyran produced the lactone in good efficiency. Acyclic compounds bearing one aryl group were oxidized in the benzylic position with moderate yields. It is important to note that the benzyl bearing with silyl group and acetoxyl group and even free toluene were over-oxidized to produce the benzoic acid in moderate yields (Table 3, entries 4–6). Interestingly, by oxidation of 1,2-diphenylethane and benzyl ether, the corresponding carboxylic acid was obtained in 46% and 40% yields, respectively (Table 3, entries 7 and 8). By-products were not detected.

Table 2
Benzylic oxidation of diarylmethane derivatives



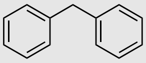
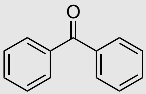
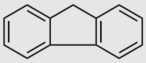
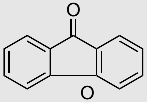
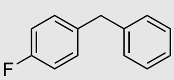
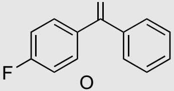
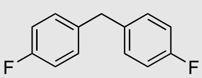
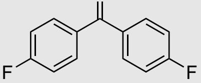
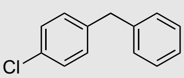
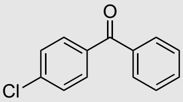
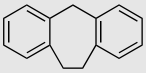
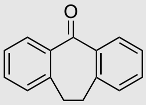
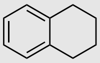
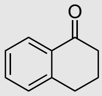
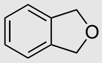
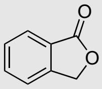
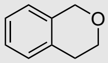
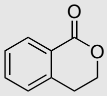
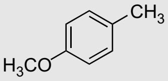
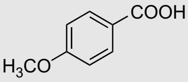
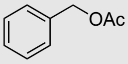
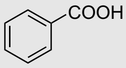
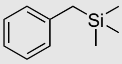
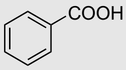
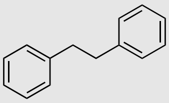
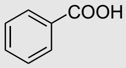
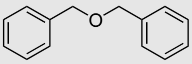
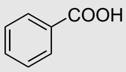
Entry	Substrate	Product	Isolated yield (%)
1			99
2			>99
3			95
4			96
5			96
6			66

Table 3
Benzylic oxidation of mono-benzylic derivatives

Entry	Substrate	Product	Isolated yield (%)
1			58
2			65
3			57
4			58
5			50
6			49
7			46
8			40

3. Conclusions

We developed a new gold-catalyzed benzylic oxidation with TBHP as oxidant resulting in the corresponding carbonyl compounds in moderate to excellent yields. It can be simply handled in air. Also, no pre-treatment of substrate and solvent are necessary. This reaction preferred to go through the radical process and study on mechanism of this reaction is underway in our laboratory.[10]

4. Experimental

4.1. Materials

All reagents were purchased from commercial suppliers and used without further purification. The substrates were commercially available. TBHP (70% in decane) was obtained from Fluka. The analysis of the isolated products is in adequation with those reported in the literature.

4.2. Representative procedure for the benzylic oxidation with $KAuCl_4\cdot 0.5H_2O$ and TBHP as the oxidant: conversion of diphenylmethane

Diphenylmethane (84 mg, 0.5 mmol) was added to the solution of $KAuCl_4\cdot 0.5H_2O$ (9.7 mg, 0.025 mmol) in pyridine (0.5 mL), followed by 2 equiv of **TBHP** (5.5 M in decane; 0.18 mL, 1 mmol) under air. After the addition, the reaction mixture was heated to 90 °C and stirred for 24 h. The mixture was then allowed to cool to room temperature and poured into a 1 N solution of aqueous HCl (10 mL) in order to remove the pyridine. The organic phase was extracted with Et_2O (30 mL), washed with water, and dried over Na_2SO_4. After filtration, the solvents were evaporated. The remaining mixture was separated by column chromatography (silica gel; ethyl acetate/petroleum ether=1:20 as eluent) affording benzophenone; yield: 90 mg (99%).

Acknowledgements

We are grateful to National Science Foundation of China and Renmin University of China for financial support.

References and notes

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) Cinellu, M. A.; Minghetti, G.; Cocco, F.; Stoccoro, S.; Zucca, A.; Manassero, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6892–6895; (d) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896–7936; (e) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239–3265.
2. (a) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164–11165; (b) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978–15979; (c) Wei, C.; Li, C.-J. *J. Am. Chem. Soc.* **2003**, *125*, 9584–9585; (d) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806–11807; (e) Yao, X.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 6884–6885; (f) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem.* **2004**, *116*, 2456–2460; *Angew. Chem., Int. Ed.* **2004**, *43*, 2502–2506; (g) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415–1418; (h) Arcadi, A.; Giuseppe, S. D.; Marinelli, F.; Rossi, E. *Adv. Synth. Catal.* **2001**, *343*, 443–446; (i) Hashmi, A. S. K.; Ding, L.; Bats, J. W.; Fischer, P.; Frey, W. *Chem.—Eur. J.* **2003**, *9*, 4339–4345; (j) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802–5803; (k) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962–6963; (l) Mamane, V.; Gress, T.; Krause, H.; Furstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654–8655; (m) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858–10859; (n) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, *127*, 6966–6967; (o) Shapiro, N. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 4160–4161; For reviews, see: (p) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200–203; (q) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2005**, *44*, 6990–6993 and references therein; (r) Zhang, Y.; Donahue, J. P.; Li, C.-J. *Org. Lett.* **2007**, *9*, 627–630; (s) Kadzimirsz, D.; Hildebrandt, D.; Merz, K.; Dyker, G. *Chem. Commun.* **2006**, 661–662; (t) Shi, M.; Liu, L.-P.; Tang, J. *Org. Lett.* **2006**, *8*, 4043–4046; (u) Hashmi, A. S. K.; Rudolph, M.; Schymura, S.; Visus, J.; Frey, W. *Eur. J. Org. Chem.* **2006**, 4905–4909 and references therein; (v) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496–499; (w) Liu, B.; De Brabander, J. K. *Org. Lett.* **2006**, *8*, 4907–4910; (x) Belting, V.; Krause, N. *Org. Lett.* **2006**, *8*, 4489–4492 and references therein; (y) Akana, J. A.; Bhattacharyya, K. X.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 7736–7737.
3. (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.
4. (a) Haruta, M.; Kobayashi, T.; Sano, H.; Yamada, N. *Chem. Lett.* **1987**, *16*, 405–408; (b) Mallat, T.; Baiker, A. *Chem. Rev.* **2004**, *104*, 3037–3058; (c) Valden, M.; Lai, X.; Goodman, D. W. *Science* **1998**, *281*, 1647–1650 and references therein.
5. (a) Biella, S.; Castiglioni, G. L.; Fumagalli, C.; Prati, L.; Rossi, M. *Catal. Today* **2002**, *72*, 43–49; (b) Arcadi, A.; Giuseppe, S. D. *Curr. Org. Chem.* **2004**, *8*, 795–812; (c) Choudhary, V. R.; Jha, R.; Jana, P. *Green Chem.* **2007**, *9*, 267–272; (d) Tsunoyama, H.; Tsukuda, T.; Sakurai, H. *Chem. Lett.* **2007**, *36*, 212–213 and references therein.
6. Boring, E.; Geletii, Y. V.; Hill, C. L. *J. Am. Chem. Soc.* **2001**, *123*, 1625–1635.
7. (a) Guan, B.; Xing, D.; Cai, G.; Wan, X.; Yu, N.; Fang, Z.; Yang, L.; Shi, Z. *J. Am. Chem. Soc.* **2005**, *127*, 18004–18005; (b) Li, H.; Guan, B.; Wang, W.; Xing, D.; Fang, Z.; Wan, X.; Yang, L.; Shi, Z. *Tetrahedron* **2007**, *63*, 8430–8434.
8. (a) Tsunoyama, H.; Sakurai, H.; Negishi, Y.; Tsukuda, T. *J. Am. Chem. Soc.* **2005**, *127*, 9374–9375; (b) Abad, A.; Concepción, P.; Corma, A.; García, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 5066–5069; (c) Comotti, M.; Della Pina, C.; Matarrese, R.; Rossi, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5812–5815; (d) Enache, D. I.; Edwards, J. K.; Landon, P.; Solsona-Espriu, B.; Carley, A. F.; Herzing, A. A.; Watanabe, M.; Kiely, C. J.; Knight, D. W.; Hutchings, G. J. *Science* **2006**, *311*, 362–365.
9. Xing, D.; Guan, B.; Cai, G.; Fang, Z.; Yang, L.; Shi, Z. *Org. Lett.* **2006**, *8*, 693–696.
10. Alvaro, M.; Aprile, C.; Corma, A.; Ferrer, B.; Garcia, H. *J. Catal.* **2007**, *245*, 249–252.