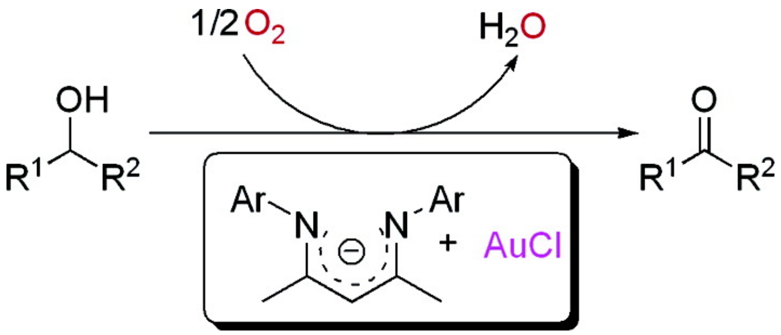
Communication

Highly Selective Aerobic Oxidation of Alcohol Catalyzed by a Gold(I) Complex with an Anionic Ligand

Bingtao Guan, Dong Xing, Guixing Cai, Xiaobin Wan, Nan Yu, Zhao Fang, Liping Yang, and Zhangjie Shi

J. Am. Chem. Soc., **2005**, 127 (51), 18004-18005• DOI: 10.1021/ja055398j • Publication Date (Web): 01 December 2005



J|A|C|S
COMMUNICATIONS

Highly Selective Aerobic Oxidation of Alcohol Catalyzed by a Gold(I) Complex with an Anionic Ligand

Bingtao Guan,[†] Dong Xing,[‡] Guixing Cai,[†] Xiaobin Wan,[†] Nan Yu,[†] Zhao Fang,[†] Liping Yang,[‡] and Zhangjie Shi*,[†]

The Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China, and Department of Chemistry, East China Normal University, Shanghai 200062, China

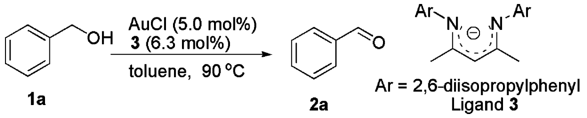
Received August 17, 2005; E-mail: zshi@pku.edu.cn

Transition metal catalyzed oxidation reactions are important processes in biological systems, organic syntheses, and industrial applications.[1] The development of new catalytic oxidation systems with economic and environmentally benign oxidants, such as dioxygen (O_2), is particularly attractive. Gold nanoparticles or clusters have been used as heterogeneous catalysts to catalyze the oxidation of CO and alcohols with O_2.[2] In 2001, Hill and his colleagues reported a homogeneous aerobic oxidation of thioethers catalyzed by Au(III) clusters in water.[3] Recently, Tsukuda and co-workers also reported the application of colloidal gold nanoclusters (Au NCs) to catalyze the aerobic oxidation of benzyl alcohols in water.[4] In contrast, a homogeneous process catalyzed by a gold species supported by organic ligands to oxidize alcohols to carbonyl products with O_2 as oxidant has never been reported despite the recent discoveries of new organic transformations catalyzed by gold species.[5] Herein we report the development of a unique gold-mediated oxidation of alcohols to aldehydes or ketones.

Studies on the structure and characteristics of gold(I) complexes were mainly focused on the linear coordination of a gold(I) species.[6] Although Bourget-Merle and co-workers reported four-coordinated gold(I) complexes with substituted bipyridine as the ligand, the reactivity of this complex has not been systematically studied.[7] Our attention was drawn upon exploring redox properties of gold complexes in solution. Initially, we tested the oxidation reaction of the reactive benzyl alcohol **1a** with gold(I) chloride supported by simple ligands, such as triphenyl phosphine, pyridine, and bipyridine in organic solvents. We found that a small amount of benzaldehyde **2a** was produced when TBHP or H_2O_2 was used as the oxidant. Although the conversion was quite low, it was promising since the result indicated the possibility of catalyzing oxygen transfer from simple oxidants via gold-mediated reactions in solutions. Further exploration led to a discovery that 30% of **2a** was produced from **1a** if neocuprione is employed as the ligand and O_2 as the oxidant in toluene (Table 1, entry 1). This result inspired us to investigate the aerobic oxidation of alcohols catalyzed by gold complexes.

On the basis of these preliminary results, we speculated that the alcohol oxidation was directly promoted by oxygenated gold species. Electron-donating ligands may help to facilitate generation of the oxidative intermediate, and a coordination saturated species should be avoided, which may shut down the oxidation chemistry. We decided to test β-diketiminate anions as the ligands. This ligand system has several advantages: (i) it bears a negative charge and is quite donating; (ii) the ligand can be prepared readily from common starting materials and has been shown to coordinate to most metal ions;[8] (iii) the flanking groups on the nitrogen atoms provide steric hindrance to leave open coordination sites on the center metal ion. For instance, we envisioned that with a bulky flanking group such as 2,6-diisopropylphenyl on the nitrogen atoms a mononuclear gold species, generated from the corresponding gold compound, could have open coordination sites to bind an oxygen transfer reagent and perhaps also substrates to facilitate the oxidation process. We tested this idea with ligand **3**. *To our delight, gold(I) chloride plus **3** serves as an excellent catalyst to oxidize benzyl alcohol **1a** to benzaldehyde **2a** in 99% GC yield with 100% conversion in toluene at 90 °C after 10 h with O_2 as the oxidant (Table 1, entry 2)*! The use of 4 Å molecular sieves is beneficial to this reaction. Further study indicated that the oxidation of **1a** also ran smoothly under air atmosphere, and the required reaction time was longer in this case (Table 1, entry 3). Catalyst loading could be decreased to 1.0 mol % under present conditions, although the catalytic efficiency was not as high as that of a previously reported process (Table 1, entry 4; as compared to up to 400 TON in the previous system).[9] TBHP and hydrogen peroxide could also be used as oxidants in the oxidation of **2a** (Table 1, entries 5 and 6); however, the efficiency of the reaction decreased obviously.

Table 1. Oxidation of Benzyl Alcohol with Gold(I) Complexes[a]



entry	oxidant	time (h)	GC conversion/ GC yield (%)
1[b]	O_2	24	30/30
2	O_2	10	100/99
3	air	24	100/99
4[c]	O_2	48	100/96
5	TBHP	24	100/96
6	H_2O_2	24	100/88

[a] Benzyl alcohol (1 mmol) was used as starting material with 5.0 mol % of AuCl and 5.0 mol % of ligand without further note under bubble pressure of O_2, N_2, or air, respectively. [b] Neocuprione (5 mol %) was used as a ligand. [c] AuCl (1.0 mol %) and **2** (1.0 mol %) were used at 10 mmol scale.

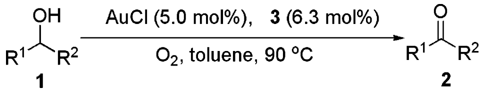
The scope of this method was illustrated with a range of alcohols. Primary and secondary benzyl and allylic alcohols all serve as good substrates (Table 2). With the use of activated primary benzyl and allylic alcohols, both conversions and yields were very high with excellent selectivity; only aldehydes were produced under the reaction conditions with no over-oxidized carboxylic acid observed. The phenyl group and alkenyl part were not oxidized by dioxygen under these conditions (Table 2, entries 1−7). Electron-donating or electron-withdrawing substitutions did not apparently affect the efficiency of the oxidation in terms of the conversion, yield, and chemoselectivity (Table 2, entries 2, 3 and 4, 5). However, the rate

---

[†] Peking University.
[‡] East China Normal University.

10.1021/ja055398j CCC: $30.25 © 2005 American Chemical Society

Table 2. Oxidation of Alcohols to Ketones/Aldehydes[a]



entry	R^1	R^2	time (h)	**2** (%)
1[c,d]	$\mathrm{C_6H_5}$	H	24	**2a** (96)
2[c]	*p*-$\mathrm{MeC_6H_4}$	H	10	**2b** (99)
3	*o*-$\mathrm{MeOC_6H_4}$	H	10	**2c** (96)
4[c]	*p*-$\mathrm{FC_6H_4}$	H	24	**2d** (99)
5	*p*-$\mathrm{BrC_6H_4}$	H	24	**2e** (92)
6	2-$\mathrm{C_{10}H_7}$	H	10	**2f** (96)
7	*trans*-$\mathrm{C_6H_5CH{=}CH}$	H	24	**2g** (94)
8[c]	$\mathrm{C_6H_5}$	$\mathrm{CH_3}$	24	**2h** (99)
9	$\mathrm{C_6H_5}$	$\mathrm{CH{=}CH_2}$	24	**2i** (96)
10	$\mathrm{C_6H_5}$	$\mathrm{C_6H_5}$	10	**2j** (99)
11	*p*-$\mathrm{NO_2C_6H_4}$	$\mathrm{CH_3}$	36	**2k** (92)
12[c]	2-thiophenyl	$\mathrm{CH_3}$	24	**2l** (86)
13[c]	$-\mathrm{CH_2CH_2CH_2CH_2CH_2}-$		24	**2m** (99)
14	$-\mathrm{CH_2CH_2CH}(t\text{-Bu})\text{-}\mathrm{CH_2CH_2}-$		24	**2n** (98)
15[c]	*n*-$\mathrm{C_7H_{15}}$	H	48	**2o** (68)[e]

[a] All reactions were carried out at 1 mmol scale. [b] Isolated yield if without further note. [c] Yield was determined by GC with *n*-decane as internal standard. [d] AuCl (1.0 mol %) and **3** (1.2 mol %) were used as catalysts at 10 mmol scale. [e] GC conversion was reported, and the major product is aldehyde, accompanied with some α,β-unsaturated aldehyde.

decreased with electron-deficient substrates (Table 2, entries 4 and 5). Methoxy and halide substitutions on the phenyl group could survive the reaction conditions, which provided good functional group tolerance (Table 2, entries 3−5). In addition, secondary benzyl and allylic alcohols could also be oxidized smoothly under the bubble pressure of oxygen, and the corresponding ketones were produced in excellent yields (Table 2, entries 8−12). Inactivated aliphatic secondary alcohols were also screened. All of the reactions ran smoothly and gave ketones as sole products in excellent yields (Table 2, entries 13 and 14). In contrast, the primary aliphatic alcohol was not a good substrate, and only moderate conversion and yield were obtained under the same condition as described above. The reaction also gave a small amount of α,β-unsaturated aldehyde through an aldol condensation process (Table 2, entry 15).

This oxidation process appears to be the cleanest oxidation process of alcohol with several different features exhibited from the previous process catalyzed by gold nanoparticles.[2a,4] First, any additive was not required during this process, and only starting material and the gold catalyst were employed to realize this oxidation with oxygen as the oxidant. After the reaction, the sole desired product was produced with water as a byproduct in most of the cases. The neutral condition was employed to realize this oxidation of alcohol, which helped avoid the competing side reactions, such as the Cannizzaro reaction. However, due to the weak Lewis acidity of the gold catalyst, the aldol condensation of aliphatic aldehyde followed by dehydration to form α,β-unsaturated aldehyde as a byproduct was observed when the primary aliphatic alcohol was utilized as a starting material and the efficiency of the oxidation was affected.

Moreover, gold particle precipitated out after several minutes in the absence of alcohol under either nitrogen or dioxygen atmosphere in this catalytic system.[10] After the precipitation of gold particles, the efficiency of oxidation was reduced dramatically. In comparison, when alcohol was added under nitrogen, the color of reaction mixture changed immediately from yellow to purple, and the solution kept relatively stable (Supporting Information, S3). The gold−ligand complex could be detected by ESI mass spectroscopy at the different stages of the reaction, even after the completion of the oxidation. Furthermore, preliminary study indicates that the reaction rate was also affected by not only the purity of dioxygen but also the concentration of the alcohol substrate. Thus, we think the oxidative process in this reaction could be different from those catalyzed by gold nanoparticles and the other reported oxidation processes.[2a,4,9,11] Further investigation to trap the intermediate of this catalytic process and elucidate the detailed mechanism is underway in our lab.

In summary, we have discovered a novel and efficient gold chemistry to catalyze a highly selective alcohol oxidation to afford a carbonyl compound with dioxygen as oxidant under simple and mild conditions. This adds a new and unique property to the existing functions of gold complexes. We hope to study the kinetics and mechanism of this reaction and explore its synthetic utilities in the future.

Acknowledgment. This research was supported by Peking University and National Science Foundation of China (No. 20542001). Acknowledgment is also made to Prof. Xi and Prof. Yang's lab for the supply of instruments and some chemicals of this research.

Supporting Information Available: Experimental details and ^{1}H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For reviews and recent references on this topic reaction, see: (a) Mellouki, A.; Le Bras, G.; Sidebottom, H. *Chem. Rev.* **2003**, *103*, 5077. (b) Adam, W.; Saha-Möller, C. R.; Ganeshpure, P. A. *Chem. Rev.* **2001**, *101*, 3499. (c) Corma, A.; Garcia, H. *Chem. Rev.* **2002**, *102*, 3837. (d) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400. (e) van Santen, R. A.; Kuipers, P. C. *Adv. Catal.* **1987**, *35*, 265. (f) Proshlyakov, D. A.; Pressler, M. A.; DeMaso, C.; Leykam, J. F.; DeWitt, D. L.; Babcock, G. T. *Science* **2000**, *290*, 1588.

(2) (a) Biella, S.; Castiglioni, G. L.; Fumagalli, C.; Prati, L.; Rossi, M. *Catal. Today* **2002**, *71*, 43. (b) Arcadi, A.; Guiseppe, S. D. *Curr. Org. Chem.* **2004**, *8*, 795. (c) Mallat, T.; Baiker, A. *Chem. Rev.* **2004**, *104*, 3037. (d) Valden, M.; Lai, X.; Goodman, D. W. *Science* **1998**, *281*, 1647. (e) Comotti, M.; Della Pina, C.; Matarrese, R.; Rossi, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5812−5815. (f) Haruta, M.; Kobayashi, T.; Sano, H.; Yamada, N. *Chem. Lett.* **1987**, *4*, 405.

(3) Boring, E.; Geletti, Y. V.; Hill, C. L. *J. Am. Chem. Soc.* **2001**, *123*, 1625.

(4) Tsunoyama, H.; Sakurai, H.; Negishi, Y.; Tsukuda, T. *J. Am. Chem. Soc.* **2005**, *127*, 9374.

(5) (a) Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526. (b) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51. (c) Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485. (d) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650. (e) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596. (f) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, *127*, 6966. (g) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164. (h) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962. (i) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387−391. (j) Wei, C.; Li, C.-J. *J. Am. Chem. Soc.* **2003**, *125*, 9584. (k) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402. (l) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415. (m) Arcadi, A.; Giuseppe, S. D.; Marinelli, F.; Rossib, E. *Adv. Synth. Catal.* **2001**, *343*, 443. (n) 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. (o) Mamane, V.; Gress, T.; Krause, H.; Furstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654.

(6) Vicente, J.; Arcas, A.; Jones, P. G.; Lautner, J. *J. Chem. Soc., Dalton Trans.: Inorg. Chem.* **1990**, 451.

(7) Cinellu, M. A.; Minghetti, G.; Stoccoro, S.; Zucca, A.; Manassero, M. *Chem. Commun.* **2004**, 1618.

(8) Yokota, S.; Tachi, Y.; Nishiwaki, N.; Ariga, M.; Itoh, S. *Chem. Rev.* **2002**, *102*, 3031.

(9) (a) Brink, G.-J. T.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636.

(10) Kundu, S.; Pal, A.; Ghosh, S. K.; Nath, S.; Panigrahi, S.; Praharaj, S.; Pal, T. *Inorg. Chem.* **2004**, *43*, 5489.

(11) (a) Marko, I. E.; Giles, P. R.; Tsukazaki, M. S.; Brown, M.; Urch, C. J. *Science* **1996**, *274*, 2044. (b) Stahl, S. S.; Thorman, J. L.; Nelson, R. C.; Kozee, M. A. *J. Am. Chem. Soc.* **2001**, *123*, 7188. (c) Mueller, J. A.; Sigman, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 7005. (d) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2001**, *123*, 7725.

JA055398J