Oxidation of Secondary Benzylic Alcohols to Ketones by Activated Carbon–Molecular Oxygen System

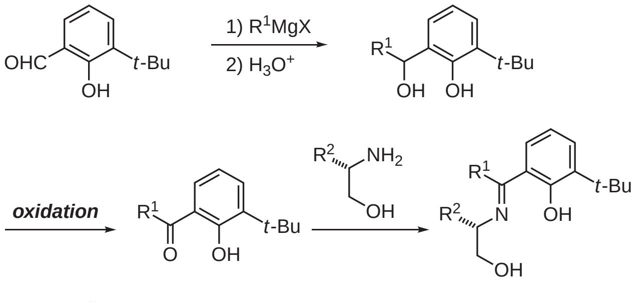
Yuki Sano, Takanori Tanaka, and Masahiko Hayashi*
Department of Chemistry, Graduate School of Science, Kobe University, Rokkodai-cho, Nada, Kobe 657-8501

(Received September 11, 2007; CL-070993; E-mail: mhayashi@kobe-u.ac.jp)

A variety of benzylic alcohols were oxidized to the corresponding carbonyl compounds selectively in the presence of activated carbon under molecular oxygen atmosphere. This process does not require any metal oxides, thus this is environmentally friendly and economical.

The transformation of alcohols into aldehydes and ketones is one of the most fundamental reactions in organic synthesis.[1] For this purpose, some stoichiometric oxidizing agents such as chromium and manganese oxides have been used so far. However, these metal salts are usually toxic and hazardous, and they often cause environmental problems. Therefore, catalytic process using oxygen or aqueous H_2O_2 as oxidizing agents by the aid of less toxic metal complex is desirable from the viewpoints of environmental concerns. Recently, Markó et al. reported an efficient catalytic system consisting of CuCl/phenanthroline/K_2CO_3/$DBADH_2$ (1,2-bis(*tert*-butoxycarbonyl)hydrazine)[2a] and TPAP (tetrapropylammonium perruthenate)/MS 4A[2b] using oxygen or air as oxidant. Noyori and his co-workers developed organic solvent- and halide-free oxidation of alcohol with aqueous H_2O_2 using Na_2WO_4 and phase-transfer catalyst (PTC) system.[2c] With regard to a Pd^{II} catalyst process, Uemura et al. reported $Pd(OAc)_2$-catalyzed oxidation of alcohols by molecular oxygen in the presence of MS 3A.[2d] A similar type of palladium-catalyzed oxidation of alcohols was also reported by Peterson and Larock.[2e]

On the other hand, during the course of our study of chiral Schiff base ligands in asymmetric reactions,[3] in order to synthesize new type of chiral Schiff base ligands (Scheme 1), we faced to necessity to develop new and efficient oxidation method for benzylic alcohol after introduction of R^1 group by Grignard reaction, because treatment of phenolic compounds with chromium oxide (CrO_3) caused the production of undesired quinolic compounds and their polymerized compounds which led the low yield of desired ketonic compounds (31–35%).[3a] We recently reported oxidative aromatization of 9,10-dihydroanthracene,[4] substituted pyrazoline,[5] dihydropyridine,[5] to the corresponding aromatic compounds by activated carbon–molecular oxygen (O_2) system. Also, we developed direct synthesis of 2-arylbenzoxazoles,[6] 2-arylbenzimidazoles,[6] and 2-arylbenzothiazoles[7] by using the same activated carbon–O_2 system. These situations have inspired us to apply this activated carbon–O_2 system to the oxidation of alcohols, and we found activated carbon–O_2 system was also effective for oxidation of some alcohols. Here, we want to report oxidation of benzylic alcohols to the corresponding ketones by activated carbon–O_2 system.[8]



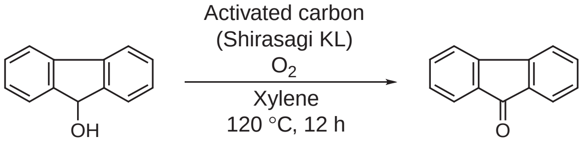
Scheme 1. Synthesis of the chiral Schiff base.

We first examined the effect of the amount of activated carbon using fluorenol as a substrate. As shown in Table 1, the presence of activated carbon is essential to promote oxidation. When the reaction was carried out in the absence of activated carbon, only 8% yield of fluorenone was obtained and 92% of starting alcohol was recovered. The choice was the use of 50 wt % of activated carbon (81% yield), though the use of 100 wt % gave higher yield (93% yield).

Then, we examined the oxidation of a variety of benzylic alcohols. Some of the obtained examples are summarized in Table 2. As shown in Table 2, various benzylic alcohols were converted to ketones. Nitrogen atom in pyridine and quinoline was not oxidized to nitrogen oxide under the present conditions (Entries 3–5). It was lucky for us, the oxidation step in our initial purpose to prepare new chiral Schiff bases, was achieved (Entries 7–10), for example, 3-*tert*-butyl-2-hydroxybenzhydrol was effectively oxidized to ketones using activated carbon–O_2 system. Unfortunately, however, even benzylic alcohols, some alcohols, such as, (2-naphthyl)phenylmethanol, 1-(2-naphthyl)-ethanol, and 1-(1-naphthyl)ethanol were unreactive to the oxidation. This is maybe due to discord between substrate (alcohol) character such as size and polarity of the molecule and micropore character of the activated carbon such as pore size, surface area, and oxygen functional group.

In conclusion, oxidation of alcohols to carbonyl compounds proceeded selectively for benzylic alcohols. Some catalytic

Table 1. Effect of amount of activated carbon in oxidation of fluorenol[a]

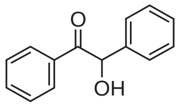
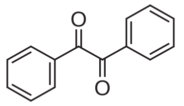
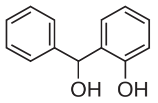
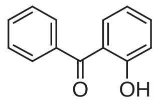
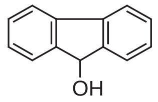
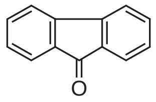
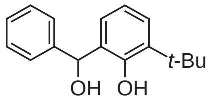
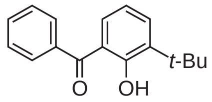
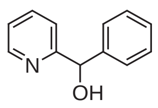
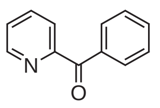
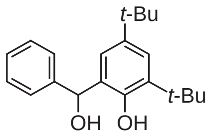
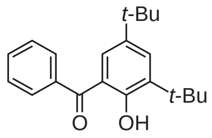
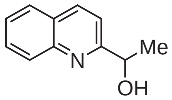
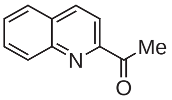
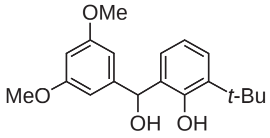
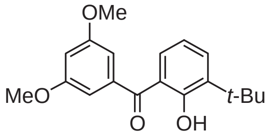
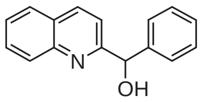
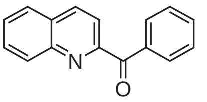
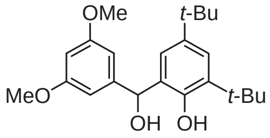
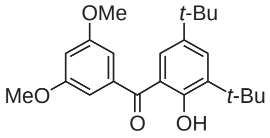


Entry	Activated carbon/wt %	Yield[b]/%
1	0	8 (92)
2	50	81 (12)
3	100	93

[a]All reactions were carried out in xylene at 120 °C for 12 h. [b]Isolated yield after silica-gel column chromatography. The values in the parentheses indicate the recovery of fluorenol.

Copyright © 2007 The Chemical Society of Japan

Table 2. Oxidation of benzylic alcohols to the corresponding carbonyl compounds by activated carbon–O_2 system[a]

Entry	Alcohol	Product	Yield[b]	Entry	Alcohol	Product	Yield[b]
1			88%	6			59%
2			81%	7			68%
3			89%	8			77%
4			88%	9			66%
5			87%	10			95%

[a]All reactions were carried out in xylene (10 mL) at 120 °C for 12 h using 500 mg of alcohol and 50 wt % of activated carbon (Shirasagi KL). [b]Isolated yield after silica-gel column chromatography.

methods do exist, using the combination of transition metal and molecular oxygen.[9] We have firstly disclosed here activated carbon–molecular oxygen system works efficiently for a variety of benzylic alcohols without any metals. Micropore in activated carbon should be believed to play an essential role in this oxidation.[10]

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas "Advanced Molecular Transformations of Carbon Resources" and No. B17340020 from the Ministry of Education, Culture, Sports, Science and Technology, Japan. T.T. is grateful to Grant-in-Aid for JSPS Fellows.

References and Notes

1 a) R. A. Sheldon, J. K. Kochi, *Metal-catalyzed Oxidations of Organic Compounds*, Academic Press, New York, **1984**. b) M. Hudlicky, *Oxidations in Organic Chemistry*, ACS Monograph Series, American Chemical Society, Washington, DC, **1990**. c) G. Tojo, M. Fernandez, *Oxidation of Alcohols to Aldehydes and Ketones*, Springer, **2006**. d) M. Hayashi, H. Kawabata, *Environmentally Benign Oxidation of Alcohols Using Transition Metal Catalysts "In Advances in Chemistry Research"*, ed. by F. L. Gerard, Nova Science Publishers, Inc, New York, **2006**, p. 45.

2 a) I. E. Markó, P. R. Giles, M. Tsukazaki, S. M. Brown, C. J. Urch, *Science* **1996**, *274*, 2044. b) I. E. Markó, P. R. Giles, M. Tsukazaki, I. Chelle–Regnaut, C. J. Urch, S. M. Brown, *J. Am. Chem. Soc.* **1997**, *119*, 12661. c) K. Sato, M. Aoki, J. Takagi, R. Noyori, *J. Am. Chem. Soc.* **1997**, *119*, 12386. d) T. Nishimura, T. Onoue, K. Ohe, S. Uemura, *Tetrahedron Lett.* **1998**, *39*, 6011. e) K. P. Peterson, R. C. Larock, *J. Org. Chem.* **1998**, *63*, 3185.

3 a) M. Hayashi, K. Tanaka, N. Oguni, *Tetrahedron: Asymmetry* **1995**, *6*, 1833. b) M. Hayashi, K. Yoshimoto, N. Hirata, K. Tanaka, N. Oguni, K. Harada, A. Matsushita, Y. Kawachi, H. Sasaki, *Isr. J. Chem.* **2001**, *41*, 241. c) T. Tanaka, Y. Yasuda, M. Hayashi, *J. Org. Chem.* **2006**, *71*, 7091.

4 N. Nakamichi, H. Kawabata, M. Hayashi, *J. Org. Chem.* **2003**, *68*, 8272.

5 a) N. Nakamichi, Y. Kawashita, M. Hayashi, *Org. Lett.* **2002**, *4*, 3955. b) N. Nakamichi, Y. Kawashita, M. Hayashi, *Synthesis* **2004**, 1015.

6 Y. Kawashita, N. Nakamichi, H. Kawabata, M. Hayashi, *Org. Lett.* **2003**, *5*, 3713.

7 Y. Kawashita, C. Ueba, M. Hayashi, *Tetrahedron Lett.* **2006**, *47*, 4231.

8 Oxidation of alcohols in gaseous phase using activated carbon. See, Y. Ohkatsu, Y. Yamazaki, K. Nagahara, T. Osa, *J. Japan Petrol. Inst.* **1979**, *22*, 129.

9 Aerobic oxidation of primary benzylic alcohols possessing hydroxy group at ortho position catalyzed by (NO)Ru-(Salen). See: A. Tashiro, A. Mitsuishi, R. Irie, T. Katsuki, *Synlett* **2003**, 1868.

10 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

Published on the web (Advance View) November 3, 2007; doi:10.1246/cl.2007.1414