Oxidation of Secondary Benzylic Alcohols to Ketones and Benzylic Oxygenation of Alkylarenes with Hydrogen Peroxide in the Presence of Activated Carbon

Shunsuke Nishida, Masahiko Hayashi*

Department of Chemistry, Graduate School of Science, Kobe University, Nada, Kobe 657-8501, Japan Fax +81(78)8035688; E-mail: mhayashi@kobe-u.ac.jp Received: 23.03.2012; Accepted after revision: 19.04.2012

Abstract: A variety of benzylic alcohols were oxidized to the corresponding carbonyl compounds selectively with 30% hydrogen peroxide (H_2O_2) in the presence of activated carbon. Alkylarenes such as fluorenes, xanthenes, and anthrone were also effectively oxygenated to the corresponding carbonyl compounds with 30% H_2O_2 as oxidant in the presence of activated carbon.

Key words: oxidation, benzylic alcohol, hydrogen peroxide, activated carbon, fluorene

Oxidation of alcohols into aldehydes and ketones is one of the most fundamental reactions in organic synthesis.¹ So far, some stoichiometric oxidizing agents such as chromium [Jones reagent,² pyridinium chlorochromate (PCC),³ pyridinium dichromate (PDC)⁴] and manganese oxides have been used for this purpose. However, these metal salts are usually toxic and hazardous and they often cause environmental problems. As the reagents without such metal oxides, Swern oxidation (DMSO/oxalyl chloride),⁵ Dess-Martin oxidation,⁶ and TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) oxidation7 have been developed. On the other hand, a catalytic process using molecular oxygen or aqueous H₂O₂ as oxidizing agents by the aid of less toxic metal complex is desirable from the viewpoints of environmental concerns. Markó et al. reported an efficient system consisting of CuCl/phenanthrocatalytic line/K₂CO₃/DBADH₂ [1,2-bis(*tert*-butoxycarbonyl)hydrazine]⁸ and TPAP(tetrapropylammonium perruthenate)/MS 4 Å⁹ using oxygen or air as oxidant. Noyori and co-workers developed organic solvent- and halide-free oxidation of alcohol with aqueous H₂O₂ using Na₂WO₄ and a phase-transfer catalyst (PTC) system.¹⁰ We also reported the oxidation of secondary benzyl and allylic alcohol leading to the formation of the corresponding ketones by Pd/C-ethylene system¹¹ and activated carbon-molecular oxygen system.12

Furthermore, direct oxygenation of alkylarenes to the corresponding carbonyl compounds is a highly important reaction because an oxygen atom can be introduced into organic substrates. For these transformations, also a stoichiometric amount of an oxidant such as manganese dioxide, chromic acid, potassium dichromate, silver oxide, selenium dioxide, and periodic acid has been employed traditionally. From the viewpoint of atom efficiency and environmental concerns, the development of methods using molecular oxygen or air has attracted much attention. In recent years, benzylic oxidation of alkylaromatics to the corresponding carbonyl compounds with molecular oxygen as oxidant using catalysts such as *N*-hydroxyphthalimide,¹³ Ru³⁺-substituted silicotungstate,¹⁴ Ru-Co-Al-CO₃ hydrotalcite,¹⁵ CuCl–2,2',3,3',5,5'-hexaphenyl-(1,1'-biphenyl)-4,4'-dioxyl,¹⁶ Co(II)–Schiff base complex¹⁷ has been reported. Methods using photooxidation¹⁸ and controlled potential electrolysis¹⁹ have also been developed.

Herein, we report the oxidation of secondary benzylic alcohols to ketones and oxygenation of alkylarenes such as fluorenes, xanthenes, and anthrone to afford the corresponding oxygenated compounds with 30% H₂O₂ in the presence of activated carbon (Scheme 1).

At first, we selected 9-fluorenol as a substrate. As we expected, 9-fluorenone was obtained in 77% yield (100 weight% of activated carbon, *m*-xylene, 95 °C, 18 h) when ten equivalents of 30% H_2O_2 were used. Less (4 equiv) and more amounts (15 equiv) of 30% H_2O_2 caused the decrease of yield (68% and 35%, respectively).

Table 1 Oxidation of 9-Fluorenol

OH OH	H ₂ O ₂ (x equiv) activated carbon (100 wt%) xylene, 95 °C, 18 h	
	X (equiv)	Yield (%) ^a
1	4	68
2	10	77
3	15	35

^a Isolated yield after silica gel column chromatography.

Then, we examined the oxidation of a variety of benzylic alcohols. Some of the obtained examples are summarized in Table 1. As shown in Table 1, various benzylic alcohols were converted into the corresponding ketones.

SYNLETT 2012, 23, 1683–1685 Advanced online publication: 13.06.2012 DOI: 10.1055/s-0031-1290367; Art ID: ST-2012-U0271-L © Georg Thieme Verlag Stuttgart · New York



Scheme 1 Oxidation of various alcohols to the corresponding carbonyl compounds



Scheme 2 Carbonylation using an activated carbon-H₂O₂ system

Thus, we have disclosed here that the activated carbon–30% H₂O₂ system works efficiently for the oxidation of a variety of benzylic alcohols without any metals. During the course of these studies, we found that a direct introduction of oxygen at the benzylic position took place. That is, treatment of fluorene with 100 weight% of activated carbon in *m*-xylene at 95 °C for 18 hours in the presence of 30% H₂O₂ afforded 9-fluorenone in 71% yield.

The results for the oxygenation of 2-substituted fluorenes and other alkylarenes with 30% H₂O₂ in the presence of activated carbon are summarized in Scheme 2. A variety of fluorene derivatives and alkylarenes such as xanthene, thioxanthene, and anthrone were employed to afford the corresponding carbonyl compounds in good to high yield (43–71% yield). It is noteworthy that the sulfur atom of thioxanthene was not oxygenated.

30% H₂O₂ was supposed to decompose to O₂ and H₂O at 95 °C in the presence of activated carbon. We think the actual oxidizing source will be O₂. Furthermore, the addition of hydroquinone to the reaction mixture retarded the reaction remarkably, so we proposed the mechanism involving radical species as shown in Scheme 3. Micropores in activated carbon should be believed to play an essential role in this oxidation.²⁰

Finally, we found that the urea $-H_2O_2$ complex is also available instead of 30% H_2O_2 , that is, the oxidation of 9fluorenol proceeded in the presence of four equivalents of urea $-H_2O_2$ and activated carbon to give 9-fluorenone in 90% yield (Scheme 4).²¹

In conclusion, we have revealed that a variety of benzylic alcohols were oxidized to the corresponding carbonyl compounds selectively with 30% hydrogen peroxide in the presence of activated carbon. Alkylarenes such as fluorenes, xanthenes, and anthrone were also effectively oxygenated to the corresponding carbonyl compounds



Scheme 3

Synlett 2012, 23, 1683-1685

© Georg Thieme Verlag Stuttgart · New York



Scheme 4

with 30% hydrogen peroxide as oxidant in the presence of activated carbon.²² It should be mentioned that we confirmed that the activated carbon was recovered and reused after drying without the loss of activity.

Acknowledgment

We acknowledge Prof. Ryosuke Matsubara of Kobe University for helpful discussion. This work was supported by a Grant-in-Aid for Scientific Research on Innovative Areas, MEXT, Japan 'Molecular Activation Directed toward Straightforward Synthesis' and No. B23350043 from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

References and Notes

- (a) Sheldon, A.; Kochi, J. K. Metal-Catalyzed Oxidations of Organic Compounds; Academic Press: New York, 1984.
 (b) Hudlicky, M. Oxidations in Organic Chemistry; ACS Monograph Series, ACS: Washington, DC, 1990. (c) Tojo, G.; Fernandez, M. Oxidation of Alcohols to Aldehydes and Ketones 2006. (d) Hayashi, M.; Kawabata, H. Environmentally Benign Oxidation of Alcohols Using Transition-Metal Catalysts, In Advances in Chemistry Research; Gerard, F. L., Ed.; Nova Science Publishers: New York, 2006, 45.
- (2) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. J. Chem. Soc. 1946, 39.
- (3) (a) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
 (b) Brown, H. C.; Rao, C. G.; Kulkarni, S. U. *J. Org. Chem.* **1979**, *44*, 2809.
- (4) Corey, E. J.; Schmidt, G. Tetrahedron Lett. 1979, 399.
- (5) Mancuso, A. J.; Swern, D. Synthesis 1981, 165.

- (6) Dess, D. B.; Martin, J. C. J. Am. Chem. Soc. 1991, 113, 7277.
- (7) Cella, J. A.; Kelley, J. A.; Kenehan, E. F. J. Org. Chem. 1975, 40, 860.
- (8) Markó, I. E.; Giles, P. R.; Tsukazaki, M.; Brown, S. M.; Urch, C. J. Science 1996, 274, 2044.
- (9) Markó, I. E.; Giles, P. R.; Tsukazaki, M.; Chelle-Regnaut, I.; Urch, C. J.; Brown, S. M. J. Am. Chem. Soc. 1997, 119, 12661.
- (10) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. J. Am. Chem. Soc. 1997, 119, 12386.
- (11) Hayashi, M.; Yamada, K.; Nakayama, S.; Hayashi, H.; Yamazaki, S. *Green Chem.* **2000**, 257.
- (12) Sano, Y.; Tanaka, T.; Hayashi, M. Chem. Lett. 2007, 36, 1414.
- (13) (a) Fukuda, O.; Sakaguchi, S.; Ishii, Y. Adv. Synth. Catal.
 2001, 343, 809. (b) Tashiro, Y.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. Adv. Synth. Catal. 2001, 343, 220. (c) Shibamoto, A.; Sakaguchi, S.; Ishii, Y. Org. Process Res. Dev. 2000, 4, 505. (d) Matsunaka, K.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. Tetrahedron Lett. 1999, 40, 2165. (e) Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T.; Nishiyama, Y. J. Org. Chem. 1995, 60, 3934.
- (14) Yamaguchi, K.; Mizuno, N. New J. Chem. 2002, 26, 972.
- (15) Matsushita, T.; Ebitani, K.; Kaneda, K. Chem. Commun. 1999, 265.
- (16) Barbiero, G.; Kim, W.-G.; Hay, A. S. *Tetrahedron Lett.* 1994, 35, 5833.
- (17) (a) Maikap, G. C.; Guhathakurta, D.; Iqbal, J. Synlett 1995, 189. (b) Punniyamurthy, T.; Iqbal, J. Tetrahedron Lett. 1994, 35, 4003.
- (18) Santamaria, J.; Jroundi, R. Tetrahedron Lett. 1991, 32, 4291.
- (19) Singh, K. N.; Singh, S. Bull. Electrochem. 2000, 16, 385.
- (20) (a) Hayashi, M. Chem. Rec. 2008, 8, 252. (b) Kawashita, Y.;
 Yanagi, J.; Fujii, T.; Hayashi, M. Bull. Chem. Soc. Jpn. 2009, 82, 482.
- (21) The detail of urea-H₂O₂-activated carbon system will be published in a separate paper.
- (22) General Experimental Procedure A mixture of alcohol (1 mmol), 100 wt% of activated carbon [Charcoal Activated, Tokyo Chemical Industry Co., Ltd (TCI)], 30% H_2O_2 (10 mmol), and anhyd xylene (10 mL) was placed in a three-necked flask. The whole was heated to 95 °C and stirred for 18 h at this temperature. After confirmation of the completion of the reaction by TLC analysis (hexane–EtOAc = 1:2), activated carbon was filtered off using Celite. The filtrate was evaporated and then silica gel column chromatographed or recrystallized to afford the carbonyl compound.

Copyright of Synlett is the property of Georg Thieme Verlag Stuttgart and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.