doi:10.1246/cl.2012.744

Pt-Catalyzed Oxidative Rearrangement of Cyclic Tertiary Allylic Alcohols to Enones Using Aqueous Hydrogen Peroxide

Takashi Nagamine, Yoshihiro Kon,* and Kazuhiko Sato*
National Institute of Advanced Industrial Science and Technology (AIST),
Tsukuba Central 5, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8565

(Received March 28, 2012; CL-120270; E-mail: y-kon@aist.go.jp)

An oxidative rearrangement of cyclic tertiary allylic alcohols to β-disubstituted α,β-unsaturated ketones by Pt black catalyst with aqueous hydrogen peroxide is described. The reaction proceeds under organic solvent- and halide-free conditions and gives only water as a coproduct. The Pt black catalyst is commercially available and can be reused at least four times.

An oxidative rearrangement of tertiary allylic alcohols to β-disubstituted α,β-unsaturated carbonyl compounds has been studied in recent decades and has been widely used in organic synthesis.[1–4] This process is an especially powerful tool for constructing β-substituted cyclic enones in natural product synthesis.[5] Moreover, β-disubstituted carbonyl compounds are very important intermediates for the enantioselective construction of all-carbon quaternary stereocenters.[6] However, until recently, stoichiometric amounts of hazardous oxochromium(VI)-based oxidants such as CrO_3, PCC, and PDC have been used exclusively as oxidants in the oxidative rearrangement of tertiary allylic alcohols.

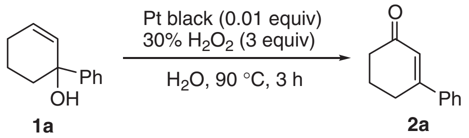
In 2004, Iwabuchi and co-workers reported that stoichiometric amounts of 2-iodylbenzoic acid (IBX) could be used instead of the hazardous Cr(VI)-based oxidant for the oxidative rearrangement of tertiary allylic alcohols.[7] In 2008, the same research group reported that 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO)-derived oxoammonium salts were more effective stoichiometric reagents for this process.[8] The catalytic oxidative rearrangement of tertiary allylic alcohols was also reported as a powerful tool for synthesizing enones by Iwabuchi and co-workers, Vatèle, and Ishihara and co-workers, independently. Iwabuchi's group demonstrated this process by using catalytic amounts of TEMPO with $NaIO_4$–SiO_2 as a co-oxidant.[9] Vatèle developed a Lewis acid-assisted oxidative rearrangement of tertiary allylic alcohols by using catalytic amounts of TEMPO with iodosylbenzene (PhIO) as a co-oxidant.[10,11] In contrast, Ishihara's group developed a 2-iodylbenzenesulfonic acid (IBS)-catalyzed oxidative rearrangement of tertiary allylic alcohols by using catalytic amounts of sodium 2-iodobenzenesulfonate with Oxone® as a co-oxidant.[12] However, the atom efficiency of these oxidants is low, and they form equimolar amounts of the deoxygenated compounds as waste.[13,14] From environmental and economical standpoints, molecular oxygen and hydrogen peroxide (H_2O_2) are ideal oxidants, because they have a high active oxygen content and the coproduct of the reactions is only water.[15] Very recently, Vatèle demonstrated an aerobic oxidative rearrangement of tertiary allylic alcohols.[11,16] In Vatèle's aerobic oxidation procedure, catalytic amounts of $CuCl_2$ (0.5 equiv) and TEMPO (0.1 equiv) are used under molecular oxygen, although high catalyst loadings are necessary to convert tertiary allylic alcohols into corresponding enones in good yields.

On the other hand, H_2O_2 is a very attractive oxidant for liquid-phase reactions, and H_2O_2 oxidation is particularly useful for the synthesis of high-value fine chemicals, pharmaceuticals, agrochemicals, and electronic materials requiring high chemical purity. Therefore, we have developed various oxidation reactions by using aqueous H_2O_2.[17] However, to our knowledge, there have been no reports on the oxidative rearrangement of tertiary allylic alcohols by using H_2O_2 as an oxidant. Herein, we report the oxidative rearrangement of cyclic tertiary allylic alcohols to β-substituted α,β-unsaturated ketones by using aqueous H_2O_2 as an oxidant and Pt black[18] as a reusable catalyst under organic solvent- and halide-free conditions.

The procedure is very simple. First, 30% aqueous H_2O_2 was added during a period of 2.5 h to a stirring mixture of 1-phenyl-2-cyclohexen-1-ol (**1a**) and Pt black[19] (0.01 equiv) in H_2O at 90 °C. The reaction mixture was continuously stirred for 0.5 h at 90 °C to give 3-phenyl-2-cyclohexen-1-one (**2a**) in 95% yield with good selectivity (95%). Dimeric ether was also obtained in 1% yield, but other presumable by-products, such as 1-phenyl-1,3-cyclohexadiene, were not observed. One of the greatest advantages of this catalytic system is that the catalyst is easily recyclable.[18,20] After the first reaction, Pt black can be recovered by simple filtration and washing, then be reused for the next reaction. Four cycles of reaction could be catalyzed by Pt black with over 90% yield of **2a** (Table 1).

Pt black was the best among our tested catalysts for the oxidative rearrangement of **1a** using H_2O_2. We examined various metal catalysts for this process, but these catalysts were less effective (Table 2). Pd black failed to afford **2a**. In the reaction using Ru black and Ir black, the yields of **2a** were low and rearranged allylic alcohol **3a** was obtained in moderate yield. Other Pt catalysts, Pt/C and $[Pt(PPh_3)_4]$, showed low catalytic activity to afford **2a** in 17% and 29% yields, respectively, with several unidentified by-products. When no catalyst was added, the reaction afforded a complex mixture containing **2a** in 10% yield. In the reaction without H_2O_2, **1a** was converted to **3a** in 47% yield and to **2a** in 2% yield with 31% recovered **1a**.

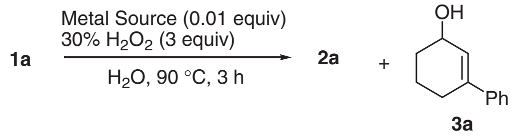
Table 1. Pt-Catalyzed oxidative rearrangement of **1a** by using 30% H_2O_2, and recycling of catalyst[a]



Run	1st	2nd	3rd	4th
Yield/%[b]	95	93	92	90

[a] 1.74 g (10 mmol) scale, H_2O (10 mL). [b] Isolated yield. See Supporting Information for details.[24]

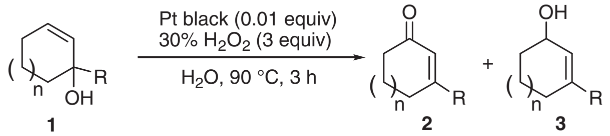
Table 2. Screening of metal source on oxidative rearrangement of **1a**[a]



Entry	Metal source	Yield/%[b]	
		2a	**3a**
1	Pt black	91	0
2	Pd black	0[c]	9[c]
3	Ru black	13	50
4	Ir black	31	27
5	5% Pt/C	17	5
6	$[Pt(PPh_3)_4]$	29	1
7[d]	—	10	5
8[e]	Pt black	2[f]	47[f]

[a]1.0 mmol scale, H_2O (1 mL). [b]Isolated yield. [c]Starting material **1a** was recovered (90%). [d]Metal source was not added. [e]H_2O_2 was not added. [f]Starting material **1a** was recovered (31%). See Supporting Information for details.[24]

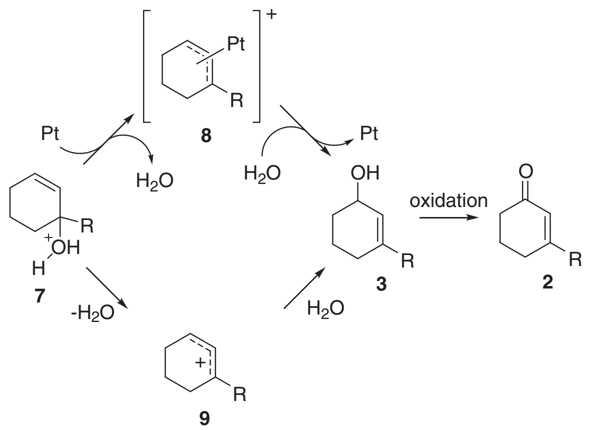
Table 3. Scope of Pt-catalyzed oxidative rearrangement[a]



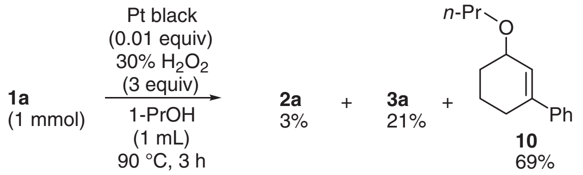
Entry	Substrate	*n*	R	Yield/%[b]	
				2	**3**
1	**1a**	1	Ph	91	0
2	**1b**	1	$4\text{-}CF_3\text{-}C_6H_4$	55	2
3	**1c**	1	$4\text{-}Cl\text{-}C_6H_4$	61	10
4	**1d**	1	$4\text{-}Me\text{-}C_6H_4$	67	9
5	**1e**	1	$4\text{-}MeO\text{-}C_6H_4$	48	0
6	**1f**	1	*n*-Bu	85	0
7	**1g**	1	*i*-Pr	78	0
8	**1h**	0	Ph	5	0
9	**1i**	2	Ph	27	10

[a]1.0 mmol scale, H_2O (1 mL). [b]Isolated yield. See Supporting Information for details.[24]

The scope and limitations of this reaction system are demonstrated in Table 3. Six-membered cyclic substrates gave the corresponding enones in moderate to high yields (Entries 1–7). Oxidations of aryl-substituted substrate, such as 4-trifluoromethylphenyl-, 4-chlorophenyl-, 4-methylphenyl-, and 4-methoxyphenyl-substituted substrates gave corresponding enones in moderate yields with several unidentified by-products (Entries 2–5). Alkyl-substituted substrates afforded corresponding enones in good yields (85% and 78% for Entries 6 and 7, respectively). Unfortunately, oxidations of five- and seven-membered cyclic substrate afforded a complex mixture, and the desired enones were obtained in low yields (5% and 27% for Entries 8 and 9, respectively). On the other hand, the reaction of 2-phenyl-3-octen-2-ol (**4**) as an example of acyclic substrate did not give desired enone, 2-phenyl-2-octen-4-one (**5**) at all, but gave rearranged allylic alcohol **6** in 35% yield with 50% recovered **4**.[21,22]



Scheme 1. Plausible reaction mechanisms of Pt-catalyzed oxidative rearrangement of tertiary allylic alcohols using H_2O_2 as oxidant.



Scheme 2. Etherification of tertially alcohol using a combination of Pt black and H_2O_2.

A plausible reaction mechanism is shown in Scheme 1. We speculate that the platinum-catalyzed oxidative rearrangement proceeds through two steps. The first is the rearrangement of the hydroxy group of **1** to **3** through the π-allylplatinum intermediate **8**.[23] Considering the acidity of H_2O_2, the elimination of the hydroxy group of **1** is assisted by H_2O_2 as a proton source. The allylic cation **9** pathway may also proceed. The second step is the oxidation of **3** using the combination of Pt black and H_2O_2.[18]

To ascertain the π-allylplatinum intermediate, we performed the following reaction (Scheme 2). To a stirring mixture of **1a** and Pt black (1 mol %) in 1-propanol at 90 °C was added 30% aqueous H_2O_2 during a period of 2.5 h. Then the reaction mixture was stirred for 0.5 h at 90 °C, to give ether **10** in 69% yield and **3a** in 21% yield. The reaction without Pt black catalyst in 1-propanol gave **10** and **3a** in low yields. These results suggest that a π-allylplatinum intermediate is formed in the presence of Pt black and H_2O_2, and the π-allylplatinum intermediate is nucleophilically attacked by 1-propanol to give ether **10**.

In conclusion, we have developed an environmentally benign and convenient process for the oxidative rearrangement of tertiary allylic alcohols to enones by using Pt black catalyst and 30% aqueous H_2O_2. This process proceeds under organic solvent- and halide-free conditions, and the catalyst is easily reusable with simple manipulation. In general, H_2O_2 oxidation with a metal catalyst seems to be environmentally benign, but it is difficult to apply a reaction that consists of multiple reaction steps that require strict control. In this study, we demonstrated that H_2O_2 oxidation can be applied to a reaction with strict control, such as oxidative rearrangement. Further mechanistic studies and application to the broad substrate are ongoing.

This work was partially supported by the New Energy and Industrial Technology Development Organization (NEDO), Japan.

References and Notes

1 For recent reviews on oxochromium(VI)-based oxidants, see: a) F. A. Luzzio, in *Organic Reactions*, ed. by L. A. Paquette, Wiley, New York, **1998**, Vol. 53, pp. 1–221. b) K. Wietzerbin, J. Bernadou, B. Meunier, *Eur. J. Inorg. Chem.* **2000**, 1391.

2 a) E. Glotter, S. Greenfield, D. Lavie, *J. Chem. Soc. C* **1968**, 1646. b) G. Büchi, B. Egger, *J. Org. Chem.* **1971**, *36*, 2021. c) P. A. Grieco, *J. Org. Chem.* **1972**, *37*, 2363. d) K. Oshima, H. Yamamoto, H. Nozaki, *J. Am. Chem. Soc.* **1973**, *95*, 4446. e) P. M. McCurry, Jr., R. K. Singh, *J. Org. Chem.* **1974**, *39*, 2316. f) J. S. Dutcher, J. G. Macmillan, C. H. Heathcock, *J. Org. Chem.* **1976**, *41*, 2663.

3 a) J. H. Babler, M. J. Coghlan, *Synth. Commun.* **1976**, *6*, 469. b) W. G. Dauben, D. M. Michno, *J. Org. Chem.* **1977**, *42*, 682. c) P. Sundararaman, W. Herz, *J. Org. Chem.* **1977**, *42*, 813.

4 a) W. G. Salmond, M. A. Barta, J. L. Havens, *J. Org. Chem.* **1978**, *43*, 2057. b) L. A. Paquette, G. D. Crouse, A. K. Sharma, *J. Am. Chem. Soc.* **1982**, *104*, 4411. c) P. S. Brown, A. B. McElroy, S. Warren, *Tetrahedron Lett.* **1985**, *26*, 249. d) A. B. McElroy, S. Warren, *Tetrahedron Lett.* **1985**, *26*, 1677. e) D. Liotta, D. Brown, W. Hoekstra, R. Monahan, III, *Tetrahedron Lett.* **1987**, *28*, 1069. f) G. Majetich, S. Condon, K. Hull, S. Ahmad, *Tetrahedron Lett.* **1989**, *30*, 1033. g) E. Öhler, E. Zbiral, *Synthesis* **1991**, 357. h) F. A. Luzzio, W. J. Moore, *J. Org. Chem.* **1993**, *58*, 2966. i) A. Nangia, P. B. Rao, *Tetrahedron Lett.* **1993**, *34*, 2681. j) G. K. S. Prakash, E. C. Tongco, T. Mathew, Y. D. Vankar, G. A. Olah, *J. Fluorine Chem.* **2000**, *101*, 199. k) B. M. Trost, A. B. Pinkerton, *J. Org. Chem.* **2001**, *66*, 7714.

5 Recent application of oxidative rearrangement to natural product synthesis. a) T. D. Bateman, A. L. Joshi, K. Moon, E. N. Galitovskaya, M. Upreti, T. C. Chambers, M. C. McIntosh, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6898. b) K. Chen, Y. Ishihara, M. M. Galán, P. S. Baran, *Tetrahedron* **2010**, *66*, 4738. c) K. C. Nicolaou, Y.-P. Sun, H. Korman, D. Sarlah, *Angew. Chem., Int. Ed.* **2010**, *49*, 5875. d) M. R. Garnsey, D. Lim, J. M. Yost, D. M. Coltart, *Org. Lett.* **2010**, *12*, 5234. e) A. Corbu, J. M. Castro, M. Aquino, Z. Gandara, P. Retailleau, S. Arseniyadis, *Eur. J. Org. Chem.* **2010**, 1483. f) L. Werner, A. Machara, T. Hudlicky, *Adv. Synth. Catal.* **2010**, *352*, 195.

6 For a review, see: C. Hawner, A. Alexakis, *Chem. Commun.* **2010**, *46*, 7295.

7 M. Shibuya, S. Ito, M. Takahashi, Y. Iwabuchi, *Org. Lett.* **2004**, *6*, 4303.

8 M. Shibuya, M. Tomizawa, Y. Iwabuchi, *J. Org. Chem.* **2008**, *73*, 4750.

9 M. Shibuya, M. Tomizawa, Y. Iwabuchi, *Org. Lett.* **2008**, *10*, 4715.

10 J.-M. Vatèle, *Synlett* **2008**, 1785.

11 J.-M. Vatèle, *Tetrahedron* **2010**, *66*, 904.

12 M. Uyanik, R. Fukatsu, K. Ishihara, *Org. Lett.* **2009**, *11*, 3470.

13 a) B. M. Trost, *Science* **1991**, *254*, 1471. b) R. A. Sheldon, *Chem. Ind. (London, U. K.)* **1992**, 903.

14 a) J. O. Metzger, *Angew. Chem., Int. Ed.* **1998**, *37*, 2975. b) P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford Unversity Press, New York, **1998**. c) W. M. Nelson, in *Green Chemical Syntheses and Processes* in *ACS Symposium Series*, ed. by P. T. Anastas, L. G. Heine, T. C. Williamson, American Chemical Society, Washington, DC, **2000**, Vol. 767, pp. 313–328. doi:10.1021/bk-2000-0767.ch024. d) M. Eissen, J. O. Metzger, E. Schmidt, U. Schneidewind, *Angew. Chem., Int. Ed.* **2002**, *41*, 414.

15 a) *Modern Oxidation Methods*, ed. by J.-E. Bäckvall, Wiley-VCH, Weinheim, Germany, **2004**. b) R. A. Sheldon, I. Arends, U. Hanefeld, *Green Chemistry and Catalysis*, Wiley-VCH, Weinheim, Germany, **2007**.

16 J.-M. Vatèle, *Synlett* **2009**, 2143.

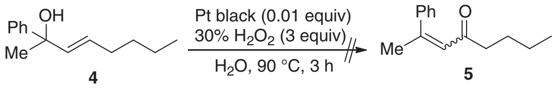
17 a) R. Noyori, M. Aoki, K. Sato, *Chem. Commun.* **2003**, 1977, and references cited therein. b) T. Chishiro, Y. Kon, K. Sato, *J. Synth. Org. Chem., Jpn.* **2008**, *66*, 1085, and references cited therein. c) Y. Kon, D. Imao, T. Nakashima, K. Sato, *Chem. Lett.* **2009**, *38*, 430. d) Y. Kon, Y. Ono, T. Matsumoto, K. Sato, *Synlett* **2009**, 1095. e) Y. Kon, H. Hachiya, Y. Ono, T. Matsumoto, K. Sato, *Synthesis* **2011**, 1092.

18 a) Y. Kon, Y. Usui, K. Sato, *Chem. Commun.* **2007**, 4399. b) Y. Kon, H. Yazawa, Y. Usui, K. Sato, *Chem.—Asian J.* **2008**, *3*, 1642.

19 We used Pt black that was purchased from N. E. CHEMCAT Co. without further pretreatment.

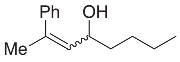
20 After the reaction, the oxidized Pt black was not observed by XPS. The stability of Pt black against H_2O_2 was commented in following paper, see: A. Kicela, S. Daniele, *Talanta* **2006**, *68*, 1632.

21 In this system, the oxidative rearrangement of **4** to **5** was not proceeded.



4 **5**

22 Rearranged allylic alcohol **6** was obtained as isomeric mixture (E:Z = 5:1). The E,Z-selectivity of allylic alcohol formation in **6** was determined by integration of ^{1}H NMR spectra recorded on a $CDCl_3$ solution of crude mixture. The relevant signals of the hydroxy methyne protons appear at δ 4.55 and 4.07, respectively.



6

23 a) M. Utsunomiya, Y. Miyamoto, J. Ipposhi, T. Ohshima, K. Mashima, *Org. Lett.* **2007**, *9*, 3371. b) T. Ohshima, Y. Miyamoto, J. Ipposhi, Y. Nakahara, M. Utsunomiya, K. Mashima, *J. Am. Chem. Soc.* **2009**, *131*, 14317.

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