Palladium(II)-Catalyzed Oxidation of Alcohols to Aldehydes and Ketones by Molecular Oxygen

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A novel combination of $Pd(OAc)_2$/pyridine/MS3A catalyzes the aerobic oxidation in toluene of a variety of primary and secondary alcohols into the corresponding aldehydes and ketones in high yields. Various substituents and protecting groups are compatible with this oxidation. The ca. 2:3 ratio of O_2 uptake to product yield is observed, whereas in the absence of MS3A, the ratio is ca. 1:1, suggesting the in situ formation of H_2O_2 and its decomposition by MS3A into water and oxygen. A catalytic cycle including the formation of a Pd(II)-alcoholate followed by β-elimination of a Pd(II)H species and a carbonyl compound and then the formation of a Pd(II)OOH species is proposed.

Introduction

The oxidation of alcohols to aldehydes and ketones is a fundamental reaction in organic synthesis.[1] For environmental and economical reasons, metal-catalyzed reactions using molecular oxygen as a reoxidant are particularly attractive. Many procedures using metal catalysts such as Ru,[2] Co,[3] Cu,[4] Pt,[5] and Rh[6] have been reported. Since the first example of the Pd-catalyzed oxidation of alcohols using molecular oxygen as a sole reoxidant in 1977, many efforts have been made to find a synthetically useful method for Pd-catalyzed oxidation.[7−10] For example, the effective aerobic oxidation of benzylic and allylic alcohols was accomplished by using Pd clusters in the presence of molecular oxygen without co-oxidants.[8] A $Pd(OAc)_2$/DMSO/O_2 catalytic method has also been reported.[9] These studies are quite interesting, but these systems are not applicable to a wide range of alcohols, especially for the effective transformation of primary and secondary aliphatic alcohols to aldehydes and ketones.

Recently, we have reported the palladium-catalyzed aerobic oxidation of some alcohols to aldehydes and ketones using a catalytic amount of $Pd(OAc)_2$, pyridine, and MS3A under oxygen atmosphere.[11] The goal for our investigation is the elaboration of an operationally simple and environmentally safe method using commercially available reagents and oxygen as a sole oxidant, which should have high selectivity, yield and compatibility with different functional groups. In this paper, we describe the full scope and some mechanistic aspects of this aerobic oxidation.

Results and Discussion

On the basis of our previous studies, aerobic oxidation of alcohols (1.0 mmol) using oxygen as an oxidant was generally carried out in the presence of $Pd(OAc)_2$ (0.05 mmol), pyridine (0.2 mmol), and MS3A (500 mg) in toluene (10 mL) under stirring at 80 °C for 2 h (a standard condition for the oxidation).

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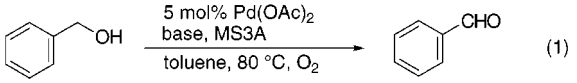
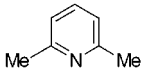
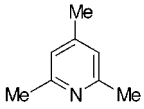
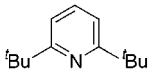
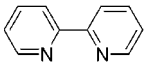
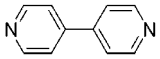
Table 1. Pd(II)-Catalyzed Oxidation of Benzyl Alcohol by Molecular Oxygen in the Presence of Various Pyridine Derivatives[a]



entry	base	conv. (%)	GLC yield[b] (%)
1		~100	quantitative
2		~100	quantitative
3		93	90
4		71	71
5		5	5
6		5	5
7		30	22

[a] Reaction conditions: $Pd(OAc)_2$ (0.05 mmol), benzyl alcohol (1.0 mmol), base (0.2 mmol), toluene (10 mL), MS3A (500 mg), O_2, 80 °C, 2 h. [b] Bibenzyl was used as an internal standard.

The rate of oxidation largely depends on the organic bases employed. Although a previous study indicated that pyridine assured the best yields of carbonyl compounds, different pyridine derivatives were examined in the oxidation of benzyl alcohol (eq 1, Table 1). 2-Substituted pyridines did not show significant differences from pyridine, but pyridines with bulky substituents at the 2,6-position were found to be less effective (Table 1, entries 2−5). Interestingly, when 2,2′-bipyridine was used, Pd was produced and the reaction did not proceed catalytically (Table 1, entry 6). Next, the effect of the amount of pyridine on the oxidation of *p*-chlorobenzyl alcohol was investigated (Figure 1). In the absence of pyridine, oxidation was slow. To achieve efficient catalytic oxidation, at least 4 molar equiv of pyridine to $Pd(OAc)_2$ is needed.

The concentration of substrates is also crucial for the successful oxidation of alcohols. When the reaction was carried out with 0.2 M of benzyl alcohol under the above-described conditions, the reaction mixture turned black and Pd was produced, resulting in slow reaction. Even in this case, the addition of excess pyridine improved the product yield and reaction rate.

Other palladium reagents, i.e., $PdCl_2$, $PdCl_2(CH_3CN)_2$, $Pd(OCOCF_3)_2$, $Pd(dba)_2$, and $Pd(PPh_3)_4$ proved ineffective. Air could be used instead of O_2, but continuous bubbling was required over long reaction times.[12] The conversion of benzyl alcohol was complete at 80 °C for 2 h, but at lower temperatures the rate of oxidation was slower. On the other hand, in refluxing toluene, the color of the reaction mixture immediately turned from yellow to black and the catalyst became deactivated. In solvents such as CH_2Cl_2, THF, Et_2O, and 1,4-dioxane the product yield greatly diminished.

(12) The oxidation of benzyl alcohol with air gave benzaldehyde in 74% yield after 2 h.

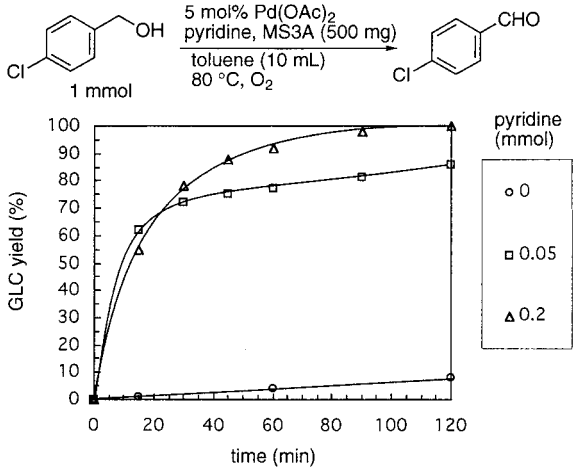


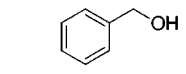
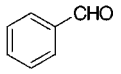
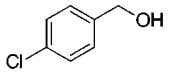
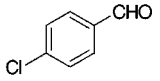
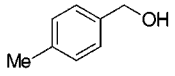
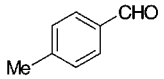
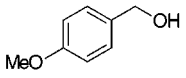
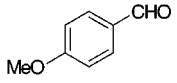
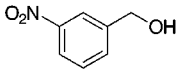
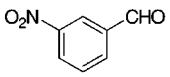
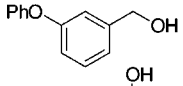
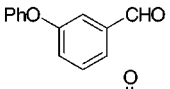
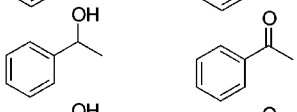
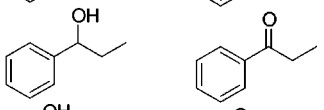
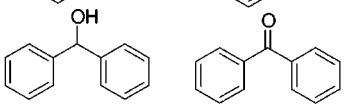
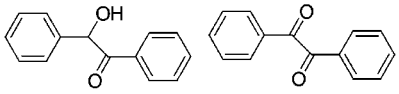
Figure 1. Time profile of the oxidation of *p*-chlorobenzyl alcohol: effect of the amount of pyridine to product yield.

Further results obtained with a wide variety of alcohols together with mechanistic considerations are described below.

Oxidation of Benzylic Alcohols. The scope of this optimized procedure for the oxidation of various benzylic alcohols is indicated by the results listed in Table 2. Primary benzylic alcohols were converted to the corresponding aldehydes in 92−96% yields within 2 h (Table 2, entries 1−8). It is noteworthy that this catalytic system shows the tolerance of a variety of substituents on aromatic nuclei. The amount of $Pd(OAc)_2$ could be reduced to 1 mol %, but a longer reaction time was required for quantitative conversion (12 h, Table 2, entry 5). For practical purposes, a slightly large-scale oxidation of *p*-methoxybenzyl alcohol (1.38 g, 10.0 mmol) was carried out to give *p*-methoxybenzaldehyde (1.29 g, 9.50 mmol, Table 2, entry 6). In the oxidation of 3-phenoxybenzyl alcohol (Table 2, entry 8), the Pd metal precipitated under the standard conditions, but the reaction again proceeded smoothly without precipitation of Pd metal when excess pyridine (1 mmol) was employed. Secondary benzylic alcohols were also easily oxidized to the corresponding ketones in high yields (Table 2, entries 9−11). However, the oxidation of benzoin was relatively slow, and the corresponding diketone was obtained in only 63% isolated yield even after 19 h (Table 2, entry 12).

Oxidation of Primary Alcohols. Next, we investigated the oxidation of the saturated primary alcohols (Table 3). Aliphatic primary alcohols were smoothly oxidized to the corresponding aldehydes selectively in high yields without any formation of carboxylic acids or their esters. The oxidation of 1-octadecanol afforded 1-octadecanal in 95% isolated yield within 2 h (Table 3, entry 1). It should be noted that this catalyst system showed the compatibility with various hydroxyl protecting groups such as tetrahydropyranyl ether (THPO, Table 3, entry 4), *tert*-butyldimethylsilyl ether (TBSO, Table 3, entries 5 and 6) and benzyl ether (BnO, Table 3, entry 7). When the oxidation by the present procedure was

Table 2. Pd(II)-Catalyzed Oxidation of Benzylic Alcohols by Molecular Oxygen[a]

entry	substrate	product	isolated yield(%)[b]	
1			quant.[c]	(100)
2			98[c]	(100)
3			95	(97)
4			96	(100)
5[d]			96	(100)
6[e]			95	(100)
7			92	(94)
8[f]			92	(97)
9			quant.[c]	(100)
10			94	(95)
11			99	(100)
12[g]			63	(71)

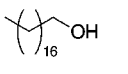
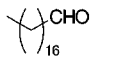
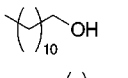
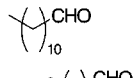
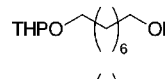
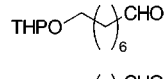
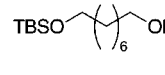
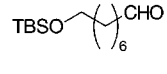
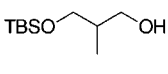
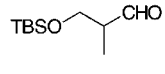
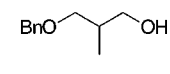
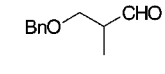
[a] Reaction conditions: $Pd(OAc)_2$ (0.05 mmol), alcohol (1.0 mmol), pyridine (0.2 mmol), MS3A (500 mg), toluene (10 mL), O_2, 80 °C, 2 h. [b] The value in parentheses is the conversion of the alcohol (%). [c] GLC yield. [d] 1 mol % $Pd(OAc)_2$, for 12 h. [e] 10-Fold scale reaction using 1 mol % $Pd(OAc)_2$ and 1.00 g of MS3A for 12 h. [f] Pyridine (1 mmol), for 5 h. [g] For 19 h.

applied to α,ω-primary diols (Table 4), the corresponding lactones were obtained in good yields as expected (entries 1−3).[13] A selective oxidative lactonization of unsymmetrical diol such as shown in entry 4 of Table 4 has been accomplished by using ruthenium[14] and rhodium[15] catalysts in the presence of a hydrogen acceptor, and in these cases the lactone **2** was obtained selectively; namely, a sterically less hindered hydroxyl group can be oxidized first, followed by the formation of lactol and then the oxidation to lactone. A similar type oxidation catalyzed by palladium using bromobenzene as cooxidant was also reported, but the selectivity was low (**1**/**2** = 62/38).[16] Unfortunately, the oxidative lactonization of unsymmetrical diol in our system did not show any chemoselectivity (Table 4, entry 4).

Oxidation of Secondary Alcohols. Secondary alcohols were also readily oxidized using the same catalytic system as summarized in Table 5. Acetate group was not affected during the reaction (Table 5, entry 4). Furthermore, even in the reaction of sterically hindered secondary alcohols such as borneol (Table 5, entry 5) and menthol (Table 5, entry 6), the corresponding ketones were obtained in high yields.

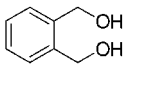
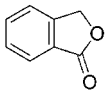
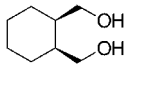
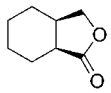
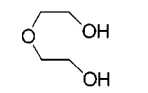
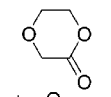
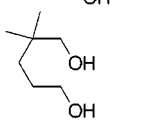
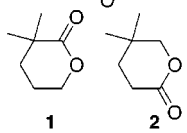
Oxidation of Alkenic Alcohols. The oxidation of alkenic alcohols including allylic ones was carried out under the same condition. The oxidation of cinnamyl alcohol was sluggish and Pd metal precipitated, resulting in a formation of only 65% of cinnamaldehyde even by prolonging the reaction time to 12 h under the identical condition (Table 6, entries 1 and 2). However, the production of Pd metal could be avoided using a quite excess of pyridine (25 times as much compared with that of the standard condition) and cinnamaldehyde was obtained in 91% isolated yield after 4 h (Table 6, entry 3). This effect suggests that the strong complexation of palladium by the alkene,[7] which might accelerate the reduction of Pd(II), could be inhibited by the coordination

Table 3. Pd(II)-Catalyzed Oxidation of Primary Alcohols by Molecular Oxygen[a]

entry	substrate	product	isolated yield(%)[b]	
1			95	(96)
2[c]			58	(61)
3			93	(97)
4			87	(93)
5[d]			92	(97)
6[d]			89	(92)
7[d]			86	(97)

[a] Reaction conditions: see footnote a of Table 2. [b] The value in parentheses is the conversion of the alcohol (%). [c] In the absence of MS3A. [d] Pyridine (1 mmol), for 4 h.

Table 4. Pd(II)-Catalyzed Oxidation of Diols by Molecular Oxygen[a]

entry	substrate	product	isolated yield(%)[b]
1			85
2			80
3			64[c]
4			91 (**1**/**2**=53/47)[d]

[a] Reaction conditions: see footnote a of Table 2. [b] Substrates were completely consumed. [c] GLC yield. [d] Determined by ^1H NMR.

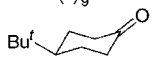
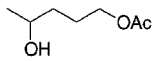
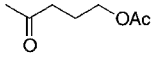
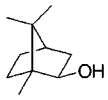
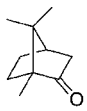
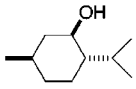
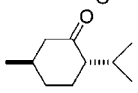
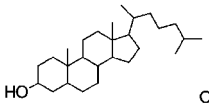
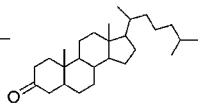
(13) Procter, G. In *Comprehensive Organic Synthesis*; Ley, S. V., Ed.; Pergamon: Oxford, U.K., 1991; Vol. 7, pp 312−318.

(14) (a) Ishii, Y.; Osakada, K.; Ikariya, T.; Saburi, M.; Yoshikawa, S. *J. Org. Chem.* **1986**, *51*, 2034. (b) Murahashi, S.-I.; Naota, T.; Ito, K.; Maeda, Y.; Taki, H. *J. Org. Chem.* **1987**, *52*, 4319.

(15) Ishii, Y.; Suzuki, K.; Ikariya, T.; Saburi, M.; Yoshikawa, S. *J. Org. Chem.* **1986**, *51*, 2822.

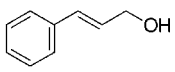
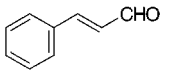
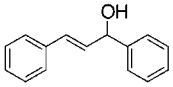
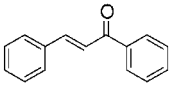
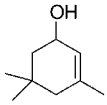
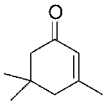
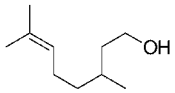
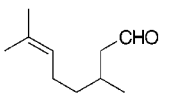
(16) Tamaru, Y.; Yamada, Y.; Inoue, K.; Yamamoto, Y.; Yoshida, Z. *J. Org. Chem.* **1983**, *48*, 1286.

Table 5. Pd(II)-Catalyzed Oxidation of Secondary Alcohols by Molecular Oxygen[a]

entry	substrate	product	isolated yield(%)[b]	
1			97	(98)
2			93	(100)
3[c]			80	(89)
4			83	(92)
5			93	(100)
6			93	(100)
7			92	(100)

[a] Reaction conditions: see footnote a of Table 2. [b] The value in parenthesis is the conversion of the alcohol (%). [c] In the absence of MS3A.

Table 6. Pd(II)-Catalyzed Oxidation of Alkenic Alcohols by Molecular Oxygen[a]

entry	substrate	product	isolated yield(%)[b]	
1			35	(46)
2[c]			66	(77)
3[d]			91	(96)
4[d]			83	(90)
5[d]			87[e]	(100)
6[f]			75	(87)
7[g]			81	(88)

[a] Reaction conditions: see footnote a of Table 2. [b] The value in parentheses is the conversion of the alcohol (%). [c] For 12 h. [d] Pyridine (5 mmol), for 4 h. [e] GLC yield. [f] For 15 h. [g] Pyridine (5 mmol), for 6 h.

of excess pyridine. Some allylic alcohols could be oxidized to the corresponding aldehydes and ketones in good yields using an excess of pyridine (Table 6, entries 4 and 5). In the oxidation of citronerol, the effect of the use of excess pyridine was small (Table 6, entries 6 and 7).

Limitations. Although it was revealed that the present catalytic system was effective for the oxidation of a wide variety of alcohols, there were some limitations for substrates to be oxidized (Figure 2). The compounds **1** and **2**, which were not oxidized with other reagents such as tetrapropylammonium perruthenate (TPAP),[2g] also failed to undergo the oxidation. The oxidation of the alcohols **3**−**5** was relatively slow, and many unidentified products were obtained in every case even using an excess of pyridine. The compounds **6** and **7** failed to be oxidized. The chemoselective oxidation between primary and secondary hydroxyl groups was attempted using

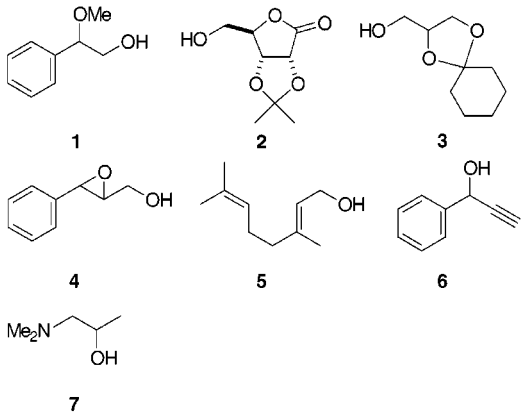
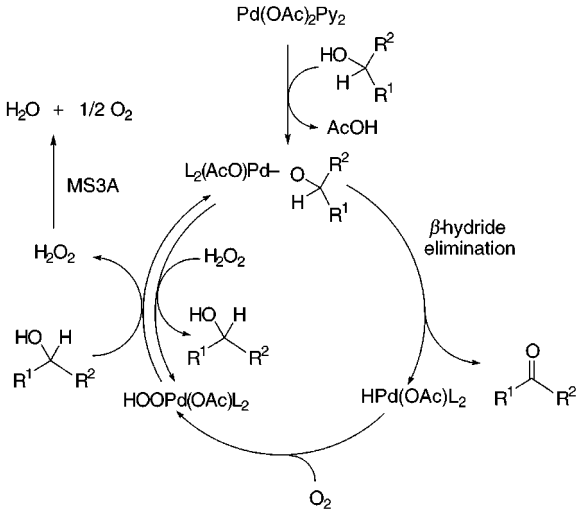


Figure 2.

Scheme 1. Plausible Reaction Pathway



some sterically hindered pyridine derivative such as 2,6-lutidine, but a significant difference in selectivity was not observed.

Reaction Pathway. We suppose that the divalent palladium complex works as an active species throughout the reaction (Scheme 1). The reaction proceeds via the formation of a Pd(II)-alcoholate[17] from an alcohol and a Pd(II)-pyridine complex[18] followed by β-elimination of a Pd(II)-hydride species from the alcoholate. The Pd(II)-hydride species can react with molecular oxygen to give a Pd(II)-hydroperoxide species,[19] and this reactive species subsequently undergoes ligand exchange with alcohol to reproduce the Pd(II)-alcoholate and H_2O_2. To detect H_2O_2 produced, the qualitative test for H_2O_2 with KI containing starch was carried out for an aqueous layer extracted from the reaction mixture (Scheme 2). The rapid change of the color from light yellow to dark blue was observed in the layer obtained from the reaction without MS3A (Scheme 2, entry 2). On the other hand, the same test was negative for that obtained from the reaction with MS3A (Scheme 2, entry 3). These results suggest that H_2O_2 is produced during the reaction and absorbed and/

(17) Tsuji, J. In *Palladium Reagents and Catalysis*; John Wiley; New York, 1995; p 105.

(18) Kravtsova, S. V.; Romm, I. P.; Stash, A. I.; Belsky, V. K. *Acta Crystallogr.* **1996**, *C52*, 2201.

(19) For the formation of a PdOOH species from a palladium species and an oxygen, see, for example: (a) Hosokawa, T.; Murahashi, S.-I. *Acc. Chem. Res.* **1990**, *23*, 49. (b) Takehira, K; Hayakawa, T.; Orita, H. *Chem. Lett.* **1985**, 1835 and references therein.

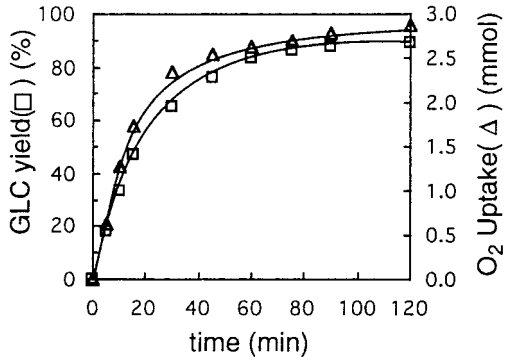


Figure 3. Time profile of the oxidation of benzyl alcohol in the absence of MS3A: the relation of yield and O_2 uptake.

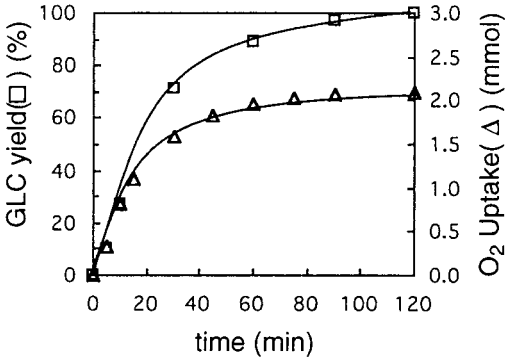
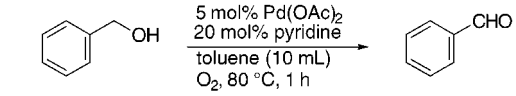
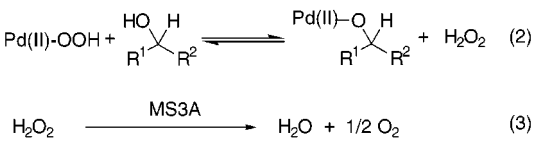


Figure 4. Time profile of the oxidation of benzyl alcohol in the presence of MS3A: the relation of yield and O_2 uptake.

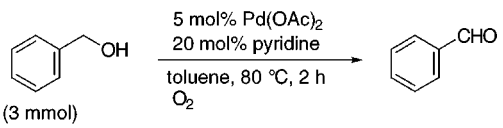
Scheme 2. Qualitative Analysis of Hydrogen Peroxide



entry	alcohol	MS3A	result of the test
1	–	–	negative
2	1 mmol	–	positive
3	1 mmol	500 mg	negative



or decomposed to O_2 and H_2O by MS3A. In fact, we separately confirmed that 30% aqueous H_2O_2 immediately decomposed to generate oxygen in toluene at 80 °C in the presence of pyridine and MS3A. The step of the ligand exchange between the Pd(II)-hydroperoxide species and alcohol would exist in equilibrium and be favorable for the Pd(II)-alcoholate under low H_2O_2 concentration because of the greater acidity of H_2O_2 relative to alcohols. Therefore, the presence of MS3A accelerated the oxidation by absorbing and/or partly decomposing H_2O_2 to O_2 and water (eqs 2 and 3, Scheme 2). Furthermore, an additional evidence for the proposed mechanism was obtained from the study of an oxygen uptake in the oxidation of benzyl alcohol (eq 4). In the oxidation of benzyl alcohol without MS3A, ca. 1:1 ratio of the oxygen uptake to benzaldehyde yield was observed (Figure 3), whereas ca. 2:3 ratio was measured when the reaction was carried out in the presence of MS3A, showing the in situ formation of oxygen during the oxidation (Figure 4).



(4)

Although the role of pyridine bases is unknown, we suppose that pyridines coordinate with Pd(II) to stabilize the Pd(II)-hydride species preventing reductive elimination of HX.

Conclusion. A system of simple combination of commercially available reagents, $Pd(OAc)_2$/pyridine/MS3A, has shown a high catalytic activity for aerobic oxidation of benzylic and aliphatic alcohols using O_2 as a sole reoxidant. The reaction has been revealed to be compatible with various substituents and protecting groups.

Experimental Section

^1H NMR spectra were obtained in $CDCl_3$ at 270 or 400 MHz with Me_4Si as an internal standard. ^{13}C NMR spectra were obtained at 67.8 or 100 MHz.

Materials. $Pd(OAc)_2$ and $PdCl_2$ were purchased from Wako Pure Chemical Ind., Ltd., and used without further purification. $Pd(OCOCF_3)_2$,[20] $Pd(dba)_2$[21] (dba = dibenzylideneacetone), and $Pd(PPh_3)_4$[22] were synthesized by the literature methods. Pyridine and other bases were purchased and used without further purification. Solvents were dried and distilled by known methods. MS3A was commercially available from Aldrich Chemical Co., Inc., which was activated by calcination just before use. All of the alcohols except six described below were commercially available and purified by normal methods just before use. Each compound prepared by known method was purified by column chromatography on silica gel (eluents, hexane−ethyl acetate).

8-(Tetrahydropyran-2-yl)oxy-1-octanol (Table 3, entry 4). The compound was prepared by the protection of one hydroxyl group of 1,8-octanediol (1 equiv of dihydropyran and montmorillonite K10 in CH_2Cl_2):[23] colorless oil; ^1H NMR (400 MHz) δ 1.26−1.90 (m, 19H), 3.38 (dt, J = 9.3, 6.8 Hz, 1H), 3.47−3.54 (m, 1H), 3.64 (t, J = 6.8 Hz, 2H), 3.74 (dt, J = 9.8, 6.8 Hz, 1H), 3.87 (ddd, J = 10.8, 8.4, 3.2 Hz, 1H), 4.57 (dd, J = 4.4, 2.7 Hz, 1H); ^{13}C NMR (100 MHz) δ 19.7, 25.5, 25.7, 26.2, 29.4, 29.4, 29.7, 30.8, 32.8, 62.4, 63.1, 67.7, 98.9.

8-*tert*-Butyldimethylsilyloxy-1-octanol (Table 3, entry 5). The compound was prepared by the protection of one hydroxyl group of 1,8-octanediol (1 equiv of *tert*-butylchlorodimethylsilane and imidazole in dimethylformamide):[24] colorless oil; ^1H NMR (400 MHz) δ 0.03 (s, 6H), 0.86 (s, 9H), 1.20−1.58 (m, 12H), 1.96 (br s, 1H), 3.57 (t, J = 7.2 Hz, 2H), 3.58 (t, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz) δ −5.3, 18.3, 25.6, 25.9, 29.3, 32.7, 32.8, 62.8, 63.2.

3-*tert*-Butyldimethylsilyloxy-2-methyl-1-propanol (Table 3, entry 6). The compound was similarly prepared from 2-methyl-1,3-propanediol (1 equiv of *tert*-butylchlorodimethylsilane and imidazole in dimethylformamide):[24] colorless oil; ^1H NMR (400 MHz) δ 0.01 (s, 6H), 0.79 (d, J = 6.8 Hz, 3H), 0.84 (s, 9H), 1.79−1.92 (m, 1H), 3.09 (br s, 1H), 3.49 (dd, J = 9.6, 8.0 Hz, 1H), 3.53−3.54 (m, 2H), 3.64 (dd, J = 9.6, 4.4 Hz, 1H); ^{13}C NMR (100 MHz) δ −5.7, 13.0, 18.1, 25.7, 37.1, 67.6, 68.1.

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3-Benzyloxy-2-methyl-1-propanol (Table 3, entry 7). The compound was prepared from 2-methyl-1,3-propanediol with NaH and benzyl bromide:[25] colorless oil; ^{1}H NMR (400 MHz) δ 0.87 (d, J = 7.3 Hz, 3H), 1.97−2.11 (m, 1H), 2.70 (br s, 1H), 3.42 (dd, J = 9.1, 7.8 Hz, 1H), 3.51 (dd, J = 9.1, 7.9 Hz, 1H), 3.57 (dd, J = 10.8, 6.3 Hz, 1H), 3.60 (dd, J = 10.8, 4.9 Hz, 1H), 4.50 (s, 2H), 7.23−7.36 (m, 5H); ^{13}C NMR (100 MHz) δ 13.4, 35.5, 67.7, 73.4, 75.3, 127.6, 127.7, 128.4, 138.0.

2,2-Dimethyl-1,5-pentanediol (Table 4, entry 4). The compound was prepared by the hydroboration−oxidation of 2,2-dimethyl-4-pentenal: colorless oil; ^{1}H NMR (270 MHz) δ 0.89 (s, 6H), 1.25−1.35 (m, 2H), 1.48−1.60 (m, 2H), 1.87 (br s, 2H), 3.33 (s, 2H), 3.64 (t, J = 6.3 Hz, 2H); ^{13}C NMR (100 MHz) δ 24.0, 27.0, 34.3, 34.8, 63.6, 71.3.

5-Acetoxy-2-pentanol (Table 5, entry 4). The compound was prepared by the protection of a primary hydroxyl group of 1,4-pentanediol with acetic anhydride in pyridine:[26] colorless oil; ^{1}H NMR (400 MHz) δ 1.21 (d, J = 5.9 Hz, 3H), 1.50 (td, J = 7.8, 5.9 Hz, 2H), 1.62−1.83 (m, 2H), 2.05 (s, 3H), 2.07 (br s, 1H), 3.83 (qt, J = 5.9, 5.9 Hz, 1H), 4.09 (t, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz) δ 21.0, 23.6, 25.0, 35.5, 64.6, 67.5, 171.3.

General Procedure for Pd(OAc)$_2$-Catalyzed Oxidation of Alcohols Using Molecular Oxygen. A typical experimental procedure is as follows: to a mixture of Pd(OAc)$_2$ (0.05 mmol) and toluene (6 mL) in a 20 mL two-necked flask were added pyridine (0.2 or 5 mmol) and MS3A (500 mg). The brown suspension turned to a yellow-white suspension when pyridine was added. Oxygen gas was introduced into the flask from an O_2-balloon under atmospheric pressure, and the mixture was heated to 80 °C for ca. 10 min. Then, an alcohol (1 mmol) in toluene (4 mL) was added using a syringe pump, and the mixture was stirred for 2 h (or appropriate time) at 80 °C under oxygen. After the reaction, the mixture was filtered through a pad of Florisil. Removal of the solvent under the reduced pressure left an oily residue, which was subjected to column chromatography (eluents, hexane-diethyl ether) to provide a product. Products obtained were determined by ^{1}H and ^{13}C NMR and GC/MS. GLC yields were determined using bibenzyl as an internal standard.

8-(Tetrahydropyran-2-yl)oxyoctanal (Table 3, entry 4): colorless oil; ^{1}H NMR (400 MHz) δ 1.10−1.90 (m, 16H), 2.41 (td, J = 7.2, 2.0 Hz, 2H), 3.37 (dt, J = 9.2, 6.8 Hz, 1H), 3.45−3.53 (m, 1H), 3.72 (dt, J = 9.2, 6.8 Hz, 1H), 3.86 (ddd, J = 10.8, 7.2, 3.6 Hz, 1H), 4.56 (dd, J = 4.4, 3.0 Hz, 1H), 9.75 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz) δ 19.7, 22.0, 25.5, 26.0, 29.1, 29.2, 29.7, 30.8, 43.9, 62.4, 67.5, 98.9, 202.8.

8-*tert*-Butyldimethylsiloxyoctanal (Table 3, entry 5): colorless oil; ^{1}H NMR (400 MHz) δ 0.03 (s, 6H), 0.88 (s, 9H), 1.24−1.37 (m, 6H), 1.45−1.66 (m, 4H), 2.41 (td, J = 7.2, 2.0 Hz, 2H), 3.58 (t, J = 7.2 Hz, 2H), 9.75 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz) δ −5.3, 18.4, 22.0, 25.6, 26.0, 29.1, 32.7, 43.9, 63.2, 202.8.

3-*tert*-Butyldimethylsiloxy-2-methylpropanal (Table 3, entry 6): colorless oil; ^{1}H NMR (400 MHz) δ 0.05 (s, 6H), 0.88 (s, 9H), 1.09 (d, J = 7.3 Hz, 3H), 2.48−2.56 (m, 1H), 3.79 (dd, J = 10.2, 6.2 Hz, 1H), 3.87 (dd, J = 10.2, 5.4 Hz, 1H), 9.74 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz) δ −5.5, 10.3, 18.2, 25.8, 48.8, 63.4, 204,7.

3-Benzyloxy-2-methylpropanal (Table 3, entry 7): colorless oil; ^{1}H NMR (400 MHz) δ 1.13 (d, J = 6.8 Hz, 3H), 2.61−2.71 (m, 1H), 3.64 (dd, J = 9.5, 5.1 Hz, 1H), 3.68 (dd, J = 9.5, 6.6 Hz, 1H), 4.52 (s, 2H), 7.25−7.37 (m, 5H), 9.72 (d, J = 1.5 Hz, 1H); ^{13}C NMR (100 MHz) δ 10.7, 46.8, 70.1, 73.3, 127.6, 127.7, 128.4, 137.9, 203.9.

5-Acetoxy-2-pentanone (Table 5, entry 4): colorless oil; ^{1}H NMR (400 MHz) δ 1.91 (tt, J = 7.3, 6.4 Hz, 2H), 2.05 (s, 3H), 2.16 (s, 3H), 2.53 (t, J = 7.3 Hz, 2H), 4.07 (t, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz) δ 20.9, 22.8, 29.9, 39.9, 63.6, 171.0, 207.6.

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