6502 *J. Org. Chem.* **2000,** *65,* 6502−6507

Efficient Oxidation of Alcohols to Carbonyl Compounds with Molecular Oxygen Catalyzed by *N*-Hydroxyphthalimide Combined with a Co Species

Takahiro Iwahama, Yasushi Yoshino, Takashi Keitoku, Satoshi Sakaguchi, and
Yasutaka Ishii*

*Department of Applied Chemistry, Faculty of Engineering & High Technology Research Center,
Kansai University, Suita Osaka 564-8680, Japan*

ishii@ipcku.kansai-u.ac.jp

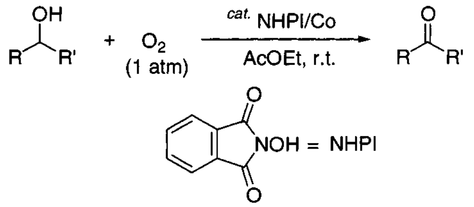
Received May 18, 2000

Highly efficient catalytic oxidation of alcohols with molecular oxygen by *N*-hydroxyphthalimide (NHPI) combined with a Co species was developed. The oxidation of 2-octanol in the presence of catalytic amounts of NHPI and $Co(OAc)_2$ under atmospheric dioxygen in AcOEt at 70 °C gave 2-octanone in 93% yield. The oxidation was significantly enhanced by adding a small amount of benzoic acid to proceed smoothly even at room temperature. Primary alcohols were oxidized by NHPI in the absence of any metal catalyst to form the corresponding carboxylic acids in good yields. In the oxidation of terminal *vic*-diols such as 1,2-butanediol, carbon−carbon bond cleavage was induced to give one carbon less carboxylic acids such as propionic acid, while internal *vic*-diols were selectively oxidized to 1,2-diketones.

Introduction

The selective oxidation of alcohols to the corresponding carbonyl compounds is a frequently used transformation in organic synthesis, and hence a wide variety of methods has been developed. Swern oxidation,[1] Dess−Martin oxidation,[2] and various metal reagents[3] are employed for this purpose. Unfortunately, these oxidations call for the use of at least a stoichiometric amount of oxidants and bring about a large quantity of noxious byproducts. From an environmental viewpoint, there has been an increasing need for selective oxidation using molecular oxygen as an oxidant under mild conditions. Although there have been many catalytic methods for the aerobic oxidation of alcohols to the corresponding carbonyl compounds,[4,5] expensive metal catalysts such as ruthenium and palladium compounds must be used to complete the oxidation satisfactorily, and some oxidations are carried out in the presence of reducing agents such as aldehydes which are eventually converted into carboxylic acids. In addition, some of these catalysts are only effective for the oxidation of reactive alcohols such as benzylic and allylic alcohols. In the practical point of view, the transformation of alcohols to carbonyl compounds by an inexpensive catalyst is particularly notable, especially in industrial chemistry. Quite recently, an efficient aerobic oxidation of aliphatic alcohols catalyzed by copper complexes has been reported.[6]

In a preceding communication, we described an efficient catalytic system consisting of *N*-hydroxyphthalimide (NHPI) and a Co ion for the oxidation of alcohols and diols with molecular oxygen as an oxidant (eq 1).[7]



(1)

---

(1) (a) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165. (b) Tidwell, T. T. *Synthesis* **1990**, 857.

(2) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.

(3) (a) Klein, W. J. In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J., Jonge, C. R. H. I., Eds.; Plenum Press: New York, 1986. (b) Piancatelli, G.; Scettri, A.; D'Auria, M. *Synthesis* **1982**, 245. (c) Fetizon, M.; Golfier, M.; Mourgues, P.; Louis, J. M. In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J., Jonge, C. R. H. I., Eds.; Plenum Press: New York, 1986; pp 503−567.

(4) (a) Sheldon, R. A. In *Dioxygen Activation and Homogeneous Catalytic Oxidation*; Simandi, L. L., Ed.; Elsevier: Amsterdam, 1991; p 573. (b) James, B. R. In *Dioxygen Activation and Homogeneous Catalytic Oxidation*; Simandi, L. L., Ed.; Elsevier: Amsterdam, 1991; p 195.

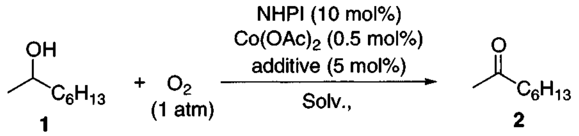
(5) Ru: (a) Tang, R.; Diamond, S. E.; Neary, N.; Mares, F. *J. Chem. Soc., Chem. Commun.* **1978**, 562. (b) Matsumoto, M.; Watanabe, N. *J. Org. Chem.* **1984**, *49*, 3435. (c) Bilgrien, C.; Davis, S.; Drago, R. S. *J. Am. Chem. Soc.* **1987**, *109*, 3786. (d) Backvall, J.-E.; Chowdhury, R. L.; Karlsson, U. *J. Chem. Soc., Chem. Commun.* **1991**, 473. (e) Murahashi, S.-I.; Naota, T.; Hirai, J. *J. Org. Chem.* **1993**, *58*, 7318. (f) Wang, G. Z.; Andreasson, U.; Backvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1994**, 1037. (g) Inokuchi, T.; Nakagawa, K.; Torii, S. *Tetrahedron Lett.* **1995**, *36*, 3223. (h) Marko, I. E.; Giles, P. R.; Tsukazaki, M.; Chelle-Regnaut, M. I.; Urch, C. J.; Brown, S. M. *J. Am. Chem. Soc.* **1997**, *119*, 12661. (i) Lenz, R.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3291. (j) Hanyu, A.; Takezawa, E.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **1998**, *39*, 5557. (k) Kaneda, K.; Yamashita, T.; Matsushita, T.; Ebitani, K. *J. Org. Chem.* **1998**, *63*, 1750. (l) Marko, I. E.; Giles, P. R.; Tsukazaki, M.; Chelle-Regnaut, M. I.; Urch, C. J.; Brown, S. M. *J. Org. Chem.* **1998**, *63*, 7576. Pd: (m) Blackburn, T. F.; Schwartz, J. *J. Chem. Soc., Chem. Commun.* **1977**, 158. (n) Kaneda, K.; Fujie, Y.; Ebitani, K. *Tetrahedron Lett.* **1997**, *38*, 9023. (o) Peterson, K. P.; Larock, R. C. *J. Org. Chem.* **1998**, *63*, 3185. (p) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **1998**, *39*, 6011. Co: (q) Yamada, T.; Mukaiyama, T. *Chem. Lett.* **1989**, 519. (r) Mandal, A. K.; Iqbal, J. *Tetrahedron Lett.* **1997**, *53*, 7641. other metals: (s) Semmelhack, M. F.; Schmid, C. R.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 3374. (t) Coleman, K. S.; Coppe, M.; Thomas, C.; Osborn, J. A. *Tetrahedron Lett.* **1999**, *40*, 3723.

(6) Marko, I. E.; Giles, P. R.; Tsukazaki, M.; Urch, C. J. *Science* **1996**, *274*, 2044.

(7) Iwahama, T.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1995**, *36*, 6923.

10.1021/jo000760s CCC: $19.00 © 2000 American Chemical Society
Published on Web 09/07/2000

Table 1. Oxidation of 2-Octanol (1) to 2-Octanone (2) with Molecular Oxygen Catalyzed by NHPI Combined with $Co(OAc)_2$ under Various Conditions[a]



run	solvent	additive[b]	temp. (°C)	time (h)	conv. (%)	yield (%)[c]
1[d]	CH_3CN	-	70	20	9	9
2	CH_3CN	-	70	20	93	93
3	AcOEt	-	70	12	84	84
4	AcOEt	MCBA	70	3	90	90
5	AcOEt	MCBA	25	20	75	75
6	AcOEt	-	25	20	21	21
7[e]	AcOEt	MCBA	25	20	62	60
8[f]	AcOEt	MCBA	25	20	75	75
9	AcOEt	BA	25	20	70	70
10	AcOEt	PMBA	25	20	67	64
11	AcOEt	PNBA	25	20	42	41

[a] **1** (3 mmol) was allowed to react with molecular oxygen (1 atm) in the presence of NHPI (10 mol %), $Co(OAc)_2$ (0.5 mol %), and additive (5 mol %) in solvent (5 mL). [b] MCBA = *m*-chlorobenzoic acid, BA = benzoic acid, PMBA = *p*-methoxybenzoic acid, PNBA = *p*-nitrobenzoic acid. [c] GC yield. [d] Without $Co(OAc)_2$. [e] MCBA (1 mol %) used. [f] MCBA (10 mol %) was used.

The NHPI used as the catalyst is a commercially available compound and can be easily prepared from phthalic anhydride, which is manufactured in large scale as a bulk chemical, and hydroxylamine.

We now find that primary and secondary alcohols can be oxidized with molecular oxygen at room temperature by the use of the NHPI combined with a Co(II) ion as the catalyst, which is very important from the viewpoint of energy-saving. In this paper, we wish to report the NHPI-catalyzed aerobic oxidation of alcohols and diols in detail.

Results

1. Oxidation of Alcohols with Molecular Oxygen. Table 1 shows representative results for the oxidation of 2-octanol (**1**) to 2-octanone (**2**) with molecular oxygen (1 atm) under various conditions. The oxidation of **1** in the presence of catalytic amounts of NHPI (10 mol %) and $Co(OAc)_2$ (0.5 mol %) in CH_3CN at 70 °C for 20 h gave **2** in high yield (93%) (run 2). From a survey of solvents, AcOEt was found to be the most efficient (run 3). In a previous paper, we showed that toluenes can be oxidized to benzoic acids by the NHPI/$Co(OAc)_2$ system under normal pressure and temperature of O_2.[8] In this oxidation, we found that an oxygenated product, benzoic acid, exerts efficient rate enhancement of the oxidation of toluenes.[9] Furthermore, even in the oxidation of alcohols by the NHPI/$Co(OAc)_2$ system, it was found that benzoic acids such as *m*-chlorobenzoic acid (MCBA) also enhance the oxidation of alcohols to carbonyl compounds. The effect of benzoic acids on the NHPI/$Co(OAc)_2$-catalyzed oxidations of alcohols will be discussed later.

Thus, the oxidation of **1** with O_2 by the NHPI/$Co(OAc)_2$ system at room temperature was induced by adding a catalytic amount of MCBA to give **2** in good yield (75%), while the same oxidation in the absence of MCBA proceeded slowly to form **2** in low yield (21%) (runs 5 and 6). To our best knowledge, the aerobic oxidation of a simple alcohol such as **1** at room temperature is only reported to be catalyzed by $Bu_4N^+RuO_4^-$, although molecular sieves 4A must be added to the reaction system.[5i] When the amount of MCBA was lowered from 5 mol % to 1 mol %, the yield of **2** slightly decreased (60%) (run 7). The oxidation using 10 mol % of MCBA was almost the same as that of 5 mol % of MCBA. (run 8). To know the substituent effect on the benzene ring in benzoic acids, benzoic acid or *p*-methoxybenzoic acid was added in place of MCBA to afford **2** in 70% and 64% yields, respectively (runs 9 and 10). However, the addition of *p*-nitrobenzoic acid resulted in a low yield of **2** (41%) compared with that of the MCBA (run 11).

On the basis of these results, various alcohols were allowed to react at room temperature using the NHPI/$Co(OAc)_2$/MCBA system under an oxygen atmosphere (Table 2).

Like 2-octanol **1**, 1-phenylethanol (**3**) was smoothly oxidized at room temperature to give acetophenone (**4**) in almost quantitative yield (run 2). Cyclic alcohols such as cyclohexanol (**5**) and cyclooctanol (**7**) were also oxidized under these conditions to the corresponding ketones, **6** and **8**, in good yields (runs 3 and 4), but *l*-menthol (**9**) was difficult to be effectively oxidized at room temperature (run 5).

A primary alcohol, 1-octanol (**13**), was oxidized to octanoic acid (**14**) in good yield (78%), although *m*CPBA was added instead of MCBA (runs 7 and 8). It is noteworthy that carboxylic acids were obtained from primary alcohols in high yields by the present oxidation, because the aerobic oxidation by metal complexes of Ru, Cu, or Pd often produces a mixture of aldehydes and carboxylic acids.[10] In our oxidation which proceeds via a free radical process as discussed later, the formed aldehydes are rapidly oxidized to carboxylic acids, since the hydrogen atom abstraction from aldehydes to acyl radicals takes place more easily than that from alcohols to α-hydroxy alkyl radicals.[11] The application of this procedure to the oxidation of lauryl alcohol (**17**) led to lauric acid (**18**) in 66% yield which can be used as a surfactant source (run 10).

On the other hand, allylic alcohol such as 1-octen-3-ol (**19**) was oxidized to α,*β*-unsaturated ketone (**20**) in moderate selectivity, probably because of the attacking of radical species to their double bonds (run 11). Needless to say, in the oxidation of a tertiary alcohol such as 1-methyl-1-cyclohexanol (**21**), no oxidation occurred and the starting **21** was recovered unchanged (run 12).

2. Oxidation of Various Diols with Molecular Oxygen. The oxidation of diols has been widely inves-

---

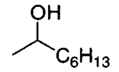
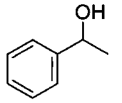
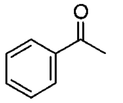
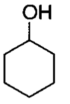
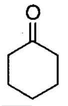
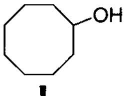
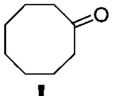
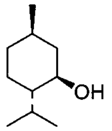
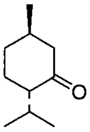
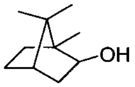
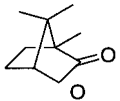
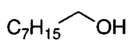
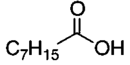
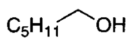
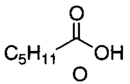
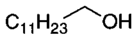
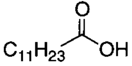
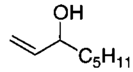
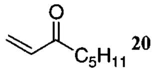
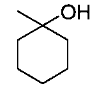
(8) Yoshino, Y.; Hayashi, Y.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 6810.

(9) For example, the oxidation of *p*-methoxytoluene in the presence of NHPI (10 mol %), $Co(OAc)_2$ (0.5 mol %), and MCBA (5 mol %) in CH_3CN at room temperature under atmospheric dioxygen for 3 h gave *p*-methoxybenzoic acid in 73% yield, although the same oxidation without MCBA produced low yield (13%) of *p*-methoxybenzoic acid.

(10) Ru and Cu complex-catalyzed aerobic oxidations of primary alcohols proceed through the formation of metal−alkoxide intermediates; see ref 5 and references therein.

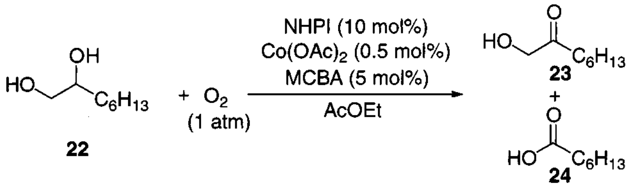
(11) Sheldon, R. A.; Kochi, J. K. In *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981.

Table 2. Oxidation of Various Alcohols with Molecular Oxygen Catalyzed by NHPI Combined with Co(OAc)$_2$ at Room Temperature[a]

run	alcohol		time (h)	conv. (%)	product		yield (%)[b]
1		**1**	20	75		**2**	75
2		**3**	15	>99		**4**	98
3		**5**	20	86		**6**	83
4		**7**	15	97		**8**	94
5		**9**	20	59		**10**	47
6		**11**	20	91		**12**	91
7		**13**	20	<1		**14**	trace
8[c]	**13**		20	79		**14**	78
9[c]		**15**	20	82		**16**	80
10[c]		**17**	15	70		**18**	66
11		**19**	20	79		**20**	67
12		**21**	20	n.r.			

[a] Alcohol (3 mmol) was allowed to react with molecular oxygen (1 atm) in the presence of NHPI (10 mol %), Co(OAc)$_2$ (0.5 mol %), and MCBA (5 mol %) in AcOEt (5 mL) at room temperature. [b] GC yield. [c] *m*CPBA (1 mol %) was used instead of MCBA.

Table 3. Oxidation of 1,2-Octanediol (22) with Molecular Oxygen[a]



run	temp. (°C)	time (h)	conv. (%)	yield (%)[b]	
				23	**24**
1	25	12	<5	trace	n.d.
2	75	12	44	27	10
3[c]	75	12	83	7	71
4[c]	75	6	41	20	13
5[d]	75	12	<10	5	n.d.

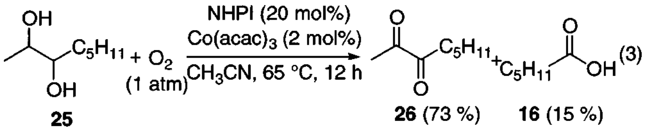
[a] **22** (3 mmol) was allowed to react with molecular oxygen (1 atm) in the presence of NHPI (10 mol %), Co(OAc)$_2$ (0.5 mol %), and additive (5 mol %) in AcOEt (5 mL). [b] GC yield. For runs 2 to 4, heptanal was confirmed as a side product. [c] Co(acac)$_3$ (1 mol %) was used instead of Co(OAc)$_2$ in CH$_3$CN. [d] Co(OAc)$_2$ (1 mol %) was used without MCBA.

tigated in oxidation chemistry, since the selective oxidation of *vic*-diols to α-ketols, diketones, or cleaved products (aldehydes or carboxylic acids) is an important transformation in organic synthesis.[12] Recently, hydrogen peroxide has been shown to be a useful oxidant for these transformations.[13] However, there is only a limited number of reports on the oxidation of diols by molecular oxygen as the oxidant.[14] In particular, the radical type of oxidation of diols with O$_2$ is rarely reported.[15] Therefore, investigating the oxidation of diols via a radical process seems to be an interesting subject from both mechanistic and synthetic aspects. Thus, we examined the aerobic oxidation of various diols by the NHPI catalyst.

The oxidation of 1,2-octanediol (**22**) was carried out under several reaction conditions (Table 3). Although secondary alcohols were successfully oxidized even at room temperature by the use of the NHPI/Co(OAc)$_2$/MCBA system, the oxidation of **22** under the same conditions formed a trace amount of 1-hydroxy-2-octanone (**23**) after 12 h (run 1). Interestingly, when Co(acac)$_3$ was used instead of Co(OAc)$_2$, the oxidation proceeded smoothly to give a one carbon less oxidized product, heptanoic acid (**24**), in good selectivity (run 3). Until now, there is no report on the selective cleavage of 1,2-diols to carboxylic acids with molecular oxygen. In this oxidation, the main product was found to be 1-hydroxy-2-octanone (**23**) at the early stage of the reaction (run 4). This indicates that a precursor to carboxylic acid **24** is α-ketol **23**. Indeed, the oxidation of **23** under these conditions led to **24** in good yield (eq 2).

$$\mathbf{23} + \underset{(1\ \mathrm{atm})}{\mathrm{O_2}} \xrightarrow[\mathrm{CH_3CN,\ 75\ °C,\ 12\ h}]{\mathrm{NHPI\ (10\ mol\%)},\ \mathrm{Co(acac)_3\ (1.0\ mol\%)}} \mathbf{24}\ (81\ \%) \qquad (2)$$

On the other hand, it was found that internal *vic*-diols such as 2,3-octanediol (**25**) are selectively oxidized to diketones such as 2,3-octanedione (**26**) rather than cleaved carboxylic acids. After the optimization of the reaction conditions, diketone **26** was obtained in 73% yield (eq 3). This is the first successful transformation of



vic-diols to diketones with O$_2$. The conversion of *vic*-diols to diketones is usually carried out by the use of metal

---

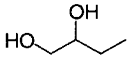
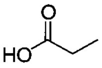
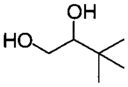
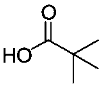
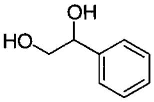
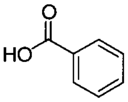
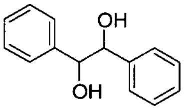
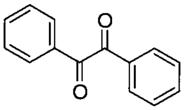
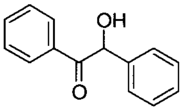
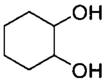
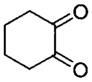
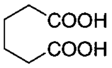
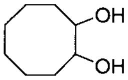
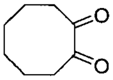
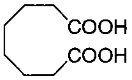
(12) Hudlicky, M. In *Oxidation in Organic Chemistry*, ACS Monograph 186; American Chemical Society: Washington, DC, 1986 and references therein.

(13) (a) Venturello, C.; Ricci, M. *J. Org. Chem.* **1986**, *51*, 1599. (b) Sakata, Y.; Ishii, Y. *J. Org. Chem.* **1991**, *56*, 6233. (c) Sakata, Y.; Katayama, Y.; Ishii, Y. *Chem. Lett.* **1992**, 671 and references therein.

(14) (a) Felthouse, T. R. *J. Am. Chem. Soc.* **1987**, *109*, 7566. (b) Okamoto, T.; Sakai, K.; Oka, S. *J. Am. Chem. Soc.* **1988**, *110*, 1187. (c) Takezawa, E.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **1999**, *1*, 713. (d) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 6750.

(15) Vries, G. D.; Schors, S. *Tetrahedron Lett.* **1968**, *9*, 5689.

Table 4. Oxidation of Various *vic*-Diols with Molecular Oxygen[a]

run	alcohol		time (h)	conv. (%)	products (%)[b]			
1		**27**	13	80		**28** 70		
2		**29**	13	89		**30** 71		
3		**31**	20	96		**32** 86		
4		**33**	20	97		**34** 84		**35** 12
5		**36**	20	62		**37** 26		**38** 30
6		**39**	20	94		**40** 42		**41** 44

[a] Diols (3 mmol) were allowed to react with molecular oxygen (1 atm) in the presence of NHPI (10 mol %) and $Co(acac)_3$ (1 mol %) in CH_3CN (5 mL). [b] GC yield.

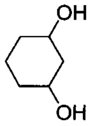
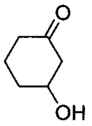
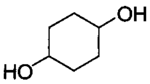
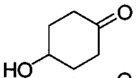
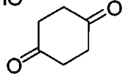
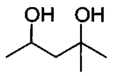
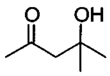
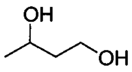
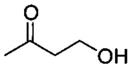
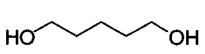
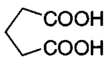
oxidants such as $AgCO_3$[16] and permanganate[17] or by the TEMPO−NaOCl system under electrochemical conditions[18] as well as by the heteropolyoxometalate-catalyzed H_2O_2 oxidation.[19]

On the basis of these results, several *vic*-diols were allowed to react using the NHPI/$Co(acac)_3$ system with molecular oxygen (1 atm) under selected reaction conditions (Table 4).

Terminal 1,2-diols such as 1,2-butanediol (**27**), 3,3-dimethyl-1,2-butanediol (**29**), and 1,2-phenylethanediol (**31**) were oxidized to the corresponding carboxylic acids, **28**, **30**, and **32**, respectively, in good yields. From 1,2-diphenylethanediol (**33**), benzyl (**34**) was obtained in 84% yield with a small amount of benzoin (**35**) (12%). However, cyclic *vis*-diols such as 1,2-cyclohexanediol (**36**) and 1,2-cyclooctanediol (**39**) were difficult to be selectively oxidized to the corresponding 1,2-diketones because of over-oxidation to dicarboxylic acids.

Table 5 shows the aerobic oxidation of several diols by the NHPI/$Co(acac)_3$ system. In contrast to the oxidation of 1,2-diols to diketones, 1,3- and 1,4-diols were oxidized to the corresponding hydroxy ketones rather than diketones in good selectivity. 1,3- and 1,4-cyclohexanediols, **42** and **44**, were converted into 3- and 4-hydroxycyclohexanones, **43** and **45**, respectively, rather than diketones, in good yields. 2-Methyl-2,4-pentanediol (**47**) and 1,3-butanediol (**49**) were oxidized to 4-hydroxy-4-methyl-2-pentanone (**48**) and 4-hydroxy-2-butanone (**50**), respectively. On the other hand, an α,ω-diol such as 1,5-pentanediol (**51**) gave a dicarboxylic acid in 66% yield. Since diols such as **51** are difficult to be oxidized to dicarboxylic acids by Ru and Pd complexes,[14d,20] the present reaction provides an alternative method for the synthesis of dicarboxylic acids from diols with molecular oxygen.

Table 5. Oxidation of Various Diols with Molecular Oxygen[a]

run	alcohol		time (h)	conv. (%)	products (%)[b]	
1		**42**	6	80		**43** 80
2		**44**	12	88		**45** 72
						**46** 16
3		**47**	12	76		**48** 75
4		**49**	12	75		**50** 61
5		**51**	20	80		**52** 66

[a] Diols (3 mmol) were allowed to react with molecular oxygen (1 atm) in the presence of NHPI (10 mol %) and $Co(acac)_3$ (1 mol %) in CH_3CN (5 mL). [b] GC yield.

Discussion

A plausible reaction path for the aerobic oxidation of **1** by the present catalytic system is illustrated in Scheme 1. In previous papers on the aerobic oxidation of alkanes

---

(16) Fetizon, M.; Golfier, M.; Louis, J. M. *J. Chem. Soc., Chem. Commun.* **1969**, 1102.

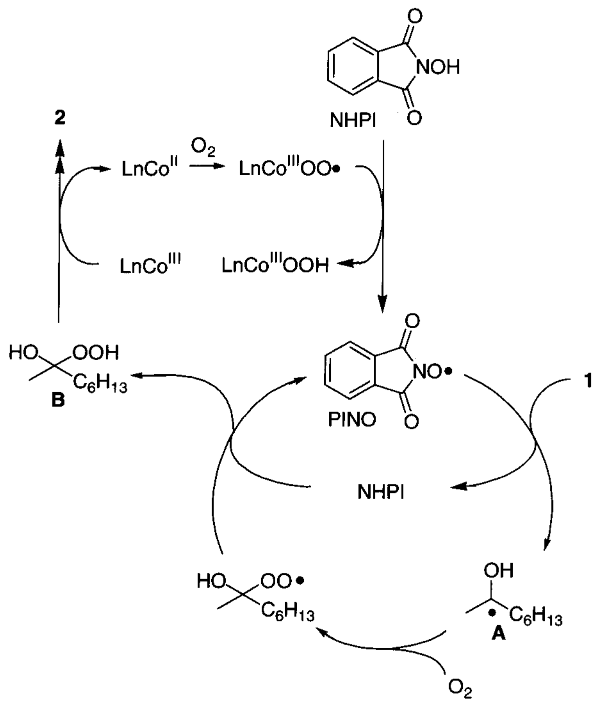
(17) Baskaran, S.; Das, J.; Chandrasekaran, S. *J. Org. Chem.* **1989**, *54*, 5182.

(18) Inokuchi, T.; Matsumoto, S.; Nishiyama, T.; Torii, S. *Synlett* **1990**, 57.

(19) Iwahama, T.; Skaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1995**, *36*, 1523.

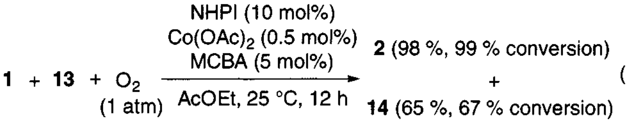
(20) Naota, T.; Takaya, H.; Murahashi, S.-I. *Chem. Rev.* **1998**, *98*, 2599 and references therein.

Scheme 1. A Possible Path for the Oxidation of 2-Octanol (1)

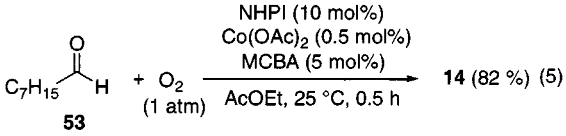


catalyzed by NHPI combined with $Co(OAc)_2$, we showed that the generation of a Co(III)−dioxygen complex, derived from the Co(II) species and O_2, is important to initiate the oxidation and that the resulting Co(III)−dioxygen complex assists the formation of a phthalimide *N*-oxyl radical (PINO) from NHPI.[8,21] The PINO radical abstracts a hydrogen atom from alkanes to form alkyl radicals which are readily trapped by O_2 to afford oxygenated products such as alcohols, ketones, and carboxylic acids. Similarly, in the present oxidation of **1**, the PINO generated from NHPI and Co(III)−dioxygen complex abstracts the hydrogen atom from **1** to form α-hydroxy carbon radical **A** which is eventually converted into ketone **2** through the formation of α-hydroxy hydroperoxide **B**.

It is thought that primary alcohols are converted into aldehydes followed by carboxylic acids through a reaction pathway similar to that of secondary alcohols. The fact that primary alcohols can be smoothly oxidized with O_2 to carboxylic acids by NHPI shows the importance of the formation of aldehydes as transient intermediates, since the aldehydes readily generate acyl radicals which serve as radical transfer agents under these reaction conditions.[11,22] It is interesting to note that the oxidation of a 1:1 mixture of primary alcohol **13** and secondary alcohol **1** afforded ketone **2** (98%) in preference to carboxylic acid **14** (65%) (eq 4), although the oxidation of **1** in the absence of **13** gave **2** in 75% yield even after 20 h (Table 1, run 5). Furthermore, the oxidation of 1-octanal (**53**) gave **14** in 82% yield even for 0.5 h (eq 5). These results show that the acyl radical and/or acylperoxy radical generated from primary alcohol **13** assists not only the formation of an α-hydroxy radical from the alcohol **1** but also the regeneration of the PINO from the NHPI.



$$\mathbf{1} + \mathbf{13} + \underset{(1\ \text{atm})}{O_2} \xrightarrow[\text{AcOEt, 25 °C, 12 h}]{\text{NHPI (10 mol\%)},\ Co(OAc)_2\ \text{(0.5 mol\%)},\ \text{MCBA (5 mol\%)}} \mathbf{2}\ \text{(98 \%, 99 \% conversion)} + \mathbf{14}\ \text{(65 \%, 67 \% conversion)} \quad (4)$$

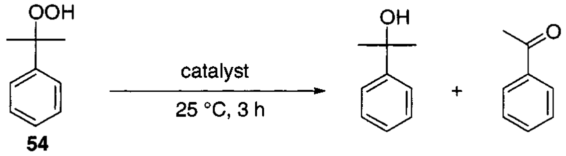


Unfortunately, it is difficult at this stage to explain clearly the role of MCBA in the aerobic oxidation by the NHPI/Co(II). However, we can make several proposals which seem to agree with the experimental data.

It is important to clarify the role of the NHPI/$Co(OAc)_2$/MCBA for the decomposition of a hydroperoxide which is formed as a precursor during the present reaction course. Thus, cumyl hydroperoxide (**54**) was chosen as a model substrate and allowed to react in the presence of a catalytic amount of $Co(OAc)_2$, $Co(OAc)_2$/MCBA, NHPI/$Co(OAc)_2$, or NHPI/$Co(OAc)_2$/MCBA at room temperature (Table 6). In contrast to the reaction of **54** by the $Co(OAc)_2$ where **54** was smoothly decomposed (run 1), **54** was not decomposed by NHPI/$Co(OAc)_2$ (run 3). These results indicate that the NHPI inhibits the decomposition of **54** by the $Co(OAc)_2$. This is believed that the NHPI reacts with $Co(OAc)_2$ to form a certain Co−NHPI complex (**55**). The visible spectrum of the acetonitrile solution of $Co(OAc)_2$ and NHPI showed a new band (λ_{max} at ca. 420 nm) probably based on the formation of Co−NHPI complex **55** (Figure 1). Interestingly, when a catalytic amount of MCBA was added to this NHPI/$Co(OAc)_2$ system, **54** was gradually decomposed (run 4). Furthermore, it was found that the visible spectrum of this solution gives rise to two absorption bands at ca. 420 and 570 nm (Figure 2). The former absorption band is attributed to the complex **55**, and the latter one was found to agree with the band of a complex **56** obtained from $Co(OAc)_2$ and MCBA which decomposed **54** efficiently (run 2). These observations suggest that the complex **56** derived from $Co(OAc)_2$ and MCBA promotes the decomposition of hydroperoxides.

In the metal-catalyzed autoxidation of alkanes, the decomposition rate of the formed alkylhydroperoxides by metal ions such as Co, Mn, and Cu is known to be

Table 6. Decomposition of Cumyl Hydroperoxide (54)[a]



run	catalytic system	conv. (%)
1	$Co(OAc)_2$	47
2	$Co(OAc)_2$/MCBA	66
3	NHPI/$Co(OAc)_2$	8
4	NHPI/$Co(Ac)_2$/MCBA	44

[a] **54** (3 mmol) was allowed to react with molecular oxygen (1 atm) in the presence of NHPI (10 mol %), $Co(OAc)_2$ (0.5 mol %), and MCBA (5 mol %) in CH_3CN (5 mL) at room temperature for 3 h.

---

(21) (a) Ishii, Y.; Iwahama, T.; Sakaguchi, S.; Nakayama, K.; Nishiyama, Y. *J. Org. Chem.* **1996**, *61*, 4520. (b) Sakaguchi, S.; Kato, S.; Iwahama, T.; Ishii, Y. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1237.

(22) Larkin, D. R. *J. Org. Chem.* **1990**, *55*, 1563 and references therein.

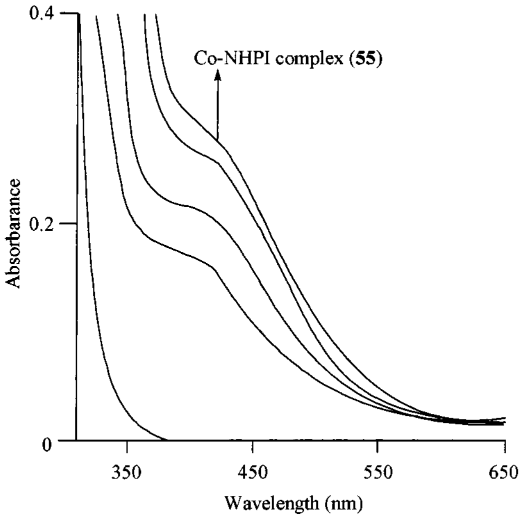


Figure 1. Visible spectra of Co−NHPI complex (**55**) obtained from NHPI and $Co(OAc)_2$. Band at 420 nm increases with increase of concentration of NHPI; $[NHPI] = 1.0 \times 10^{-4} \sim 1.5 \times 10^{-3}$ M, $[Co] = 1.0 \times 10^{-4}$ M in CH_3CN.

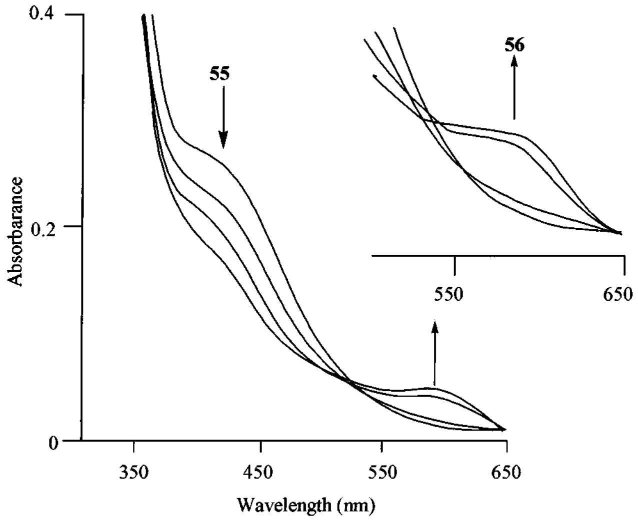


Figure 2. Visible spectra of solution consisting of NHPI, $Co(OAc)_2$, and MCBA. Absorption at 420 nm based on **55** decreases with corresponding increase at 570 nm (band of a complex (**56**) obtained from $Co(OAc)_2$ and MCBA); $[NHPI] = 1.5 \times 10^{-3}$ M, $[Co] = 1.0 \times 10^{-4}$ M, $[MCBA] = 0 \sim 3.0 \times 10^{-3}$ M in CH_3CN.

important to determine the over all reaction rate.[23] Therefore, it is reasonable to assume that MCBA reacts with $Co(OAc)_2$ to form the complex **56** which accelerates the decomposition of alkylhydroperoxides at room temperature. Thus, the aerobic oxidation of secondary alcohols by NHPI/$Co(OAc)_2$ system is facilitated by the addition of the MCBA.

In conclusion, an efficient and practical oxidation method of alcohols and diols with molecular oxygen using NHPI as the key catalyst has been developed. This reaction provides a new environmentally friendly and economical route to the conversion of alcoholic functions to carbonyl groups.

Experimental Section

General. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using $CDCl_3$ with tetramethylsilane as the internal standard. Infrared (IR) spectra were measured using NaCl or KBr pellets. Flash chromatography was performed with use of silica gel (70−230 mesh). Gas chromatography was carried out with a flame ionization detector using a 0.22 mm × 25 m capillary column. Preparative HPLC was performed on GPC columns. GC-MS spectra were obtained at an ionization energy of 70 eV. All starting materials, solvents, and catalysts were purchased from commercial sources and used without further treatment.

General Procedure for Oxidation of Alcohols. An AcOEt (5 mL) solution of 2-octanol (**1**) (3 mmol), NHPI (49 mg, 10 mol %), $Co(OAc)_2$ (3.7 mg, 0.5 mol %), and *m*-chlorobenzoic acid (23 mg, 5 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 25 °C for 20 h. Removal of the solvent under reduced pressure gave a clean liquid, which was purified by column chromatography on silica gel (*n*-hexane/AcOEt = 5/1) to give 2-octanone (**2**).

All products are commercially available and were identified through comparison of their ^1H and ^{13}C NMR or GC-MS with those of authentic samples.

General Procedure for Oxidation of 1,2-Octanediol (22). An acetonitrile (5 mL) solution of 1,2-octanediol (**22**) (3 mmol), NHPI (49 mg, 10 mol %), and $Co(acac)_3$ (10.7 mg, 1.0 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 75 °C for 12 h. The workup was performed using the previously described method.

Carboxylic acids **24**, **28**, **30**, and **32** are commercially available and were identified through comparison of their GC-MS with those of authentic samples. Hydroxy ketone **23** was identical to that described in the literature.[24]

General Procedure for Oxidation of 2,3-Octanediol (25). An acetonitrile (5 mL) solution of 2,3-octanediol (**25**) (2 mmol), NHPI (65 mg, 20 mol %), and $Co(acac)_3$ (14.2 mg, 2.0 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 65 °C for 12 h. Removal of the solvent under reduced pressure gave a clean yellow liquid, which was purified by column chromatography on silica gel (chloroform/AcOEt = 5/1) to give 2,3-octanedione (**26**).

Products **16**, **34**, **35**, **37**, **38**, **41**, **46**, **48**, and **52** are commercially available and were identified through comparison of their ^1H and ^{13}C NMR or GC-MS with those of authentic samples. Compounds **26**,[25] **40**,[26] **43**,[27] **45**,[28] and **50**[29] were identified through comparison with literature known NMR data.

Acknowledgment. This work was supported by the Japan Society for the Promotion of Science under the Research for the Future program JSPS.

JO000760S

---

[23] Haber, F.; Weiss, J. *Proc. R. Soc. London, Ser. A* **1934**, *147*, 332.

[24] Sakata, Y.; Ishii, Y. *J. Org. Chem.* **1991**, *56*, 6233.

[25] Banwell, M. G.; Bridges, V. S.; Dupuche, J. R.; Richards, S. L.; Walter, J. M. *J. Org. Chem.* **1994**, *59*, 6338.

[26] Amon, C. M.; Banwell, M. G.; Lance Gravatt, G. *J. Org. Chem.* **1987**, *52*, 4851.

[27] Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 2596.

[28] Nakano, T.; Terada, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1986**, 774.

[29] Yamawaki, K.; Yoshida, T.; Suda, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1986**, 59.