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Direct Conversion of Cyclohexane into Adipic Acid with Molecular Oxygen Catalyzed by *N*-Hydroxyphthalimide Combined with Mn(acac)$_2$ and Co(OAc)$_2$

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Abstract:

Direct conversion of cyclohexane into adipic acid was achieved by the use of the radical catalyst, *N*-hydroxyphthalimide (NHPI), in the presence of a small amount of a transition metal. For instance, cyclohexane could be converted into adipic acid in 73% selectivity at 73% conversion under atmospheric oxygen (1 atm) in the presence of NHPI (10 mol %) and Mn(acac)$_2$ (1 mol %) at 100 °C for 20 h. ESR measurements show that the formation of phthalimide *N*-oxyl generated from NHPI with O_2 was assisted by Co(II) species. Thus, the oxidation of cyclohexane to adipic acid was found to be enhanced by the addition of a small amount of Co(OAc)$_2$ to the NHPI/Mn(acac)$_2$ system. The NHPI-catalyzed oxidation of cyclohexane provides an attractive direct method which has long been desired in the chemical industry for the manufacturing of adipic acid. The present oxidation seems to be the first practical environmentally friendly process, in which nitric acid is not used as the oxidant, for the production of adipic acid from cyclohexane.

Introduction

Direct oxygenation of saturated hydrocarbons with molecular oxygen is a particularly important reaction in industrial chemistry.[1] Several transition-metal-catalyzed oxidations of alkanes by the combined use of oxygen and reducing agents such as H_2,[2] NaBH$_4$,[3] RCHO,[4] etc., have been reported. Recently, halogenated metalloporphyrins have been shown to be efficient catalysts for oxygenation of alkanes such as isobutane with oxygen without any co-reductant to give alcohols and/or carbonyl compounds.[5] However, the development of new efficient methods for the catalytic aerobic oxidation of alkanes and cycloalkanes is one of the most challenging subjects in oxidation chemistry.

The oxidation of hydrocarbons such as cyclohexane and xylenes is currently carried out on a commercial scale worldwide by homogeneous liquid-phase oxidation in the presence of Co and/or Mn salts, which process is commonly referred to as autoxidation.[6] Autoxidation of cyclohexane produces a mixture of cyclohexanone/cyclohexanol (K/A oil) as major products along with a small amount of adipic acid.[6] The resulting K/A oil is oxidized to adipic acid which is the most important compound of all aliphatic dicarboxylic acids manufactured. Current technology for the industrial production of adipic acid involves the two-step oxidation of cyclohexane,[7] i.e., aerobic oxidation of cyclohexane at 150−170 °C in the presence of a soluble Co catalyst to form a K/A oil from which subsequent nitric oxidation produces adipic acid. However, the conversion of cyclohexane in the first step is necessary to keep only 3−6% in order to obtain higher selectivity to the K/A oil, and the second step results in a large amount of undesired NOx which are environmentally critical compounds. Therefore, there has been an increasing need for the direct one-step conversion of cyclohexane to adipic acid with molecular oxygen due to these environmental and economical concerns, although the oxidation of cyclohexane to adipic acid has been described under oxygen pressure using a higher concentration of Co(III) acetate under the influence of aldehyde or cyclohexanone which serves as promoter of the autoxidation.[8]

In previous reports, we have described that *N*-hydroxyphthalimide (NHPI), which serves as the radical catalyst,

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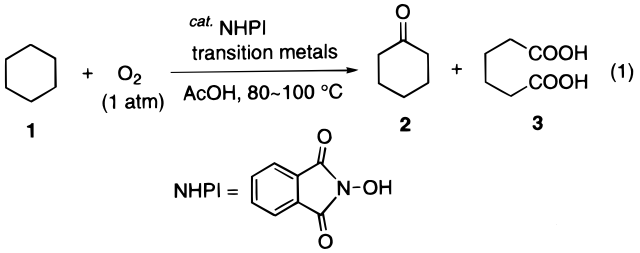
Table 1. **Oxidation of cyclohexane (1) with molecular oxygen catalyzed by NHPI in the presence of various transition metals**[a]

run	metal salt	convn (%)	selectivity (%) 2	selectivity (%) 3
1		<1	trace	n.d.
2[b]		13	53	20
3[c]		14	65	21
4[d]	Mn(acac)$_2$	<1	trace	n.d.
5	Mn(acac)$_2$	36	20	46
6	Mn(OAc)$_2$	35	13	45
7[d]	Co(acac)$_2$	<1	trace	n.d.
8	Co(acac)$_2$	36	35	35
9	Co(OAc)$_2$	40	36	34
10[d]	Cr(acac)$_3$	<1	n.d.	n.d.
11	Cr(acac)$_3$	38	33	25
12[d]	[Rh(OAc)$_2$]$_2$	<1	trace	n.d.
13	[Rh(OAc)$_2$]$_2$	40	39	25
14	Cu(acac)$_2$	14	71	12
15	Fe(acac)$_3$	5	99	n.d.
16	Ni(acac)$_2$	<1	trace	n.d.
17	Zn(acac)$_2$	15	47	4
18	Ti(acac)$_2$	5	99	n.d.

[a] Compound **1** (3 mmol) was allowed to react with oxygen (1 atm) in the presence of NHPI (10 mol %) and transition metal (0.5 mol %) in acetic acid (7.5 ml) at 100 °C for 6. [b] Reaction was carried out for 20 h. [c] Reaction was carried out under oxygen pressure (10 atm) in CH$_3$CN. [d] In the absence of NHPI.

promotes the aerobic oxidation of benzylic compounds,[9] cycloalkanes,[10] alkylbenzenes,[11] polycyclic alkanes,[12] and alcohols[13] in the presence or absence of Co(acac)$_n$ ($n = 2$ or 3) under mild conditions. In this paper, we report in detail the one-step oxidation of cyclohexane (**1**) to adipic acid (**3**) with molecular oxygen (1 atm) catalyzed by NHPI combined with transition metal salts (eq 1).



Results and Discussions

1. Oxidation of Cycloalkanes by NHPI/Mn(II)−O$_2$ System. Table 1 shows representative results for the oxidation of **1** with molecular oxygen by NHPI in the presence of various transition metals. The oxidation of **1** under atmospheric oxygen (1 atm) by NHPI (10 mol %) and Mn(acac)$_2$ (0.5 mol %) at 100 °C (run 5, Table 1) gave cyclohexanone (**2**) (20%) and **3** (46%) as main products in higher conversion (36%) compared with that of the conventional autoxidation. The addition of Co(acac)$_2$, Co(OAc)$_2$, Cr(acac)$_3$, or [Rh(OAc)$_2$]$_2$ to the NHPI-catalyzed oxidation of **1** resulted in **2** (33−39%) and **3** (25−35%) in 36−40% conversions (runs 8, 9, 11, and 13, Table 1). In contrast, Cu(acac)$_2$, Fe(acac)$_2$, Ni(acac)$_2$, Zn(acac)$_2$, and Ti(acac)$_2$ were less efficient catalysts in the present oxidation. Needless to say, **1** was difficult to oxidize by either NHPI or a transition metal alone under these conditions (runs 1, 4, 7, 10, and 12, Table 1). Although cyclohexanol (**4**) is expected to be formed in this oxidation, only a trace amount of **4** was obtained. In a previous paper, we showed that alcohols can be oxidized to the corresponding carbonyl compounds by the NHPI-catalyzed aerobic oxidation.[13] Hence, it is believed that the resulting **4** was easily oxidized to **2** and/or **3** in the present system, although alcohols are generally difficult to oxidize to ketones by the conventional autoxidation.

Table 2. **Oxidation of 1 with molecular oxygen catalyzed by NHPI in the presence of Mn(acac)$_2$ under various conditions**[a]

run	time (h)	convn (%)	selectivity (%) 2	selectivity (%) 3
1	6	36	20	46
2	14	49	18	71
3[b]	14	42	19	65
4	20	65	2	65
5[c]	20	55	trace	68
6[d]	14	61	trace	71
7[d,e]	20	73	trace	73
8[f]	20	<5	trace	n.d.
9[g]	20	70	trace	60
10[h]	20	75	trace	68

[a] Compound **1** (3 mmol) was allowed to react under oxygen (1 atm) in the presence of NHPI (10 mol %) and Mn(acac)$_2$ (0.5 mol %) in acetic acid (7.5 mL) at 100 °C. [b] Reaction was carried out at 80 °C. [c] NHPI (5 mol %) was used. [d] Mn(acac)$_2$ (1.0 mol %) was used. [e] Glutaric acid (**5**) (9%), succinic acid (**6**) (6%), cyclohexyl acetate (**7**) (up to 2%), and cyclohexanol (**4**) (up to 1%) were obtained. [f] In the absence of NHPI. [g] Mn(OAc)$_2$ (1 mol %) was used. [h] Mn(OBz)$_2$ (1 mol %) was used.

It is interesting to note that manganese salts were more effective than cobalt salts for the conversion of **1** into **3**. Thus, the oxidation of **1** by NHPI combined with manganese salts under various conditions was examined (Table 2).

In the oxidation of **1** under atmospheric oxygen (1 atm) in the presence of NHPI (10 mol %) and Mn(acac)$_2$ (0.5 mol %) at 100 °C for 20 h, **3** was obtained in higher conversion (65%) and selectivity (65%) (run 4, Table 2). Even when NHPI was halved under these conditions, **1** was converted into **3** in 68% selectivity at 55% conversion (run 5, Table 2). Similar results were also obtained when the oxidation was carried out at 80 °C (run 3, Table 2). By the use of 1 mol % of Mn(acac)$_2$, **3** was obtained in higher selectivity (73%) along with small amounts of glutaric acid (**5**) (9%), succinic acid (**6**) (6%), cyclohexyl acetate (**7**) (up to 2%), and **4** (up to 1%) in 73% conversion (run 7, Table 2).[14] All balance of these oxidation products was 91%, and the lost selectivity of about 9% is believed to be due to progressive dehomologation of dicarboxylic acid as well as

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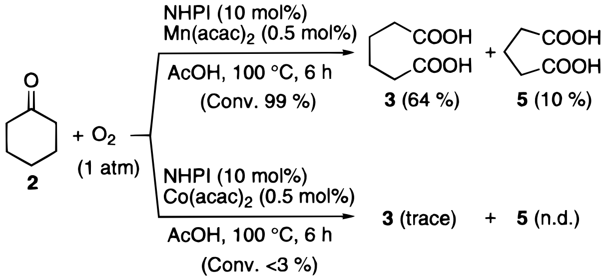
Table 3. **Oxidation of various cycloalkanes with molecular oxygen catalyzed by NHPI in the presence of Mn(acac)$_2$[a]**

run	substrate	temp (°C)	convn (%)	products, %[b]	
				cycloalkanone	dicarboxylic acid
1	cyclooctane (**9**)	100	83	cyclooctanone (**10**), 2	suberic acid (**11**), 53
2	cyclodecane (**12**)	100	90	cyclodecanone (**13**), 2	sebacic acid (**14**), 55
3	cyclododecane (**15**)	70	81	cyclododecane (**16**), 3	dodecanedioic acid (**17**), 68

[a] Substrate (3 mmol) was allowed to react under oxygen (1 atm) in the presence of NHPI (10 mol %) and Mn(acac)$_2$ (1.0 mol %) in acetic acid (7.5 mL) for 14 h. [b] Yield based on substrate reacted.

complete oxidation.[15] The oxidation of **1** by Mn(OAc)$_2$ or Mn(OBz)$_2$ as a cocatalyst gave almost the same result as that by Mn(acac)$_2$ (runs 9 and 10, Table 2). The effect of Mn(II) on the oxidation of **1** by the present system is contrast to that of manganese derivatives shown by Schulz[8c] and Tanaka.[8d] In these reactions, Co, Cr and Zn salts are reported to be good catalysts for the conversion of **1** to **3**, while Mn salts have no catalytic activity.[16]

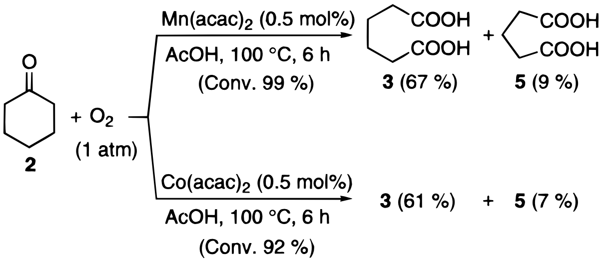
To gain further information about the effect of Co and Mn salts on the NHPI-catalyzed oxidation of **1** to **3**, cyclohexanone **2**, which would be a precursor of **3**, was oxidized under similar reaction conditions. The oxidation of **2** by NHPI (10 mol %) in the presence of Mn(acac)$_2$ (0.5 mol %) in acetic acid at 100 °C for 6 h produced **3** as the major product (64%), glutaric acid (**5**) (10%), and succinic acid (**6**) (5%) (eq 2). However, in the oxidation of **2** using NHPI/Co(acac)$_2$ and NHPI/Co(acac)$_3$ systems, most of the starting **2** was recovered unchanged (eq 2). In contrast, the same oxidation of **2** by Co(acac)$_2$ in the absence of NHPI gave 61% of **3** in 92% conversion (eq 3).



(2)

It is interesting to note that, in the oxidation of **2** by Co(acac)$_2$, the color of the solution changed from pink to dark-green, which shows the formation of a Co(III) species in the course of the reaction. However, in the oxidation of **2** in the presence of NHPI and Co(acac)$_2$, the color of the solution immediately changed from pink to orange and the color was retained during the reaction.

On the other hand, cyclohexanone (**2**) was smoothly oxidized to adipic acid (**3**) by Mn(acac)$_2$ in the presence or absence of NHPI. These observations seem to be related to the formation of a certain Co complex from Co(OAc)$_2$, **2**, and NHPI. In fact, the treatment of Co(OAc)$_2$ (0.5 mmol) with **2** (10 mmol) in the presence of NHPI (2.5 mmol) in acetic acid at 100 °C resulted in a dark-brown complex (**8**) which appears a mixture of some cobalt complexes. The aerobic oxidations of **1** and **2** using the complex **8** were examined, but both substrates were not oxidized by **8** and recovered unchanged. These results suggest that an unreactive species which serves as an inhibitor in the aerobic oxidation of **1** and **2** may be involved in the complex **8**. However, the oxidation of cyclohexanol (**4**) by the NHPI/Co(II) system led to **2** (55%) along with **3** (8%) and **7** (27%) in 69% conversion as reported previously.[13]



(3)

On the basis of these results, the aerobic oxidation of several cycloalkanes was examined using the NHPI/Mn(acac)$_2$ system (Table 3). Like **1**, cyclooctane (**9**) and cyclodecane (**12**) were oxidized to the corresponding cycloalkanones, cyclooctanone (**10**) and cyclodecanone (**13**), and dicarboxylic acids, suberic acid (**11**) and sebacic acid (**14**), respectively (runs 1 and 2, Table 3). Cyclododecane (**15**) was easily oxidized even at 70 °C to give dodecanedioic acid (**17**) in good yield along with cyclodecanone (**16**) (run 3, Table 3). These facts show that the present NHPI-catalyzed aerobic oxidation can be applied to the production of cyclic ketones and dicarboxylic acids, which are very important chemicals, of a wide variety of large-membered cycloalkanes.

2. Oxidation of Cyclohexane (1) by NHPI/Mn(II)/Co(II)−O$_2$ System. In the NHPI-catalyzed aerobic oxidation of alkylbenzenes such as toluene or ethylbenzene, we indicated that the Co(II) species is more effective than the Mn(II) species as the cocatalyst.[10,11] For instance, the oxidation of ethylbenzene (**18**) in the presence of NHPI (2 mol %) and Co(II) species (0.5 mol %) afforded acetophenone (**19**) (88% selectivity) and 1-phenylethanol (**20**) (9% selectivity) in 75% conversion of **18**, while the same oxidation using Mn(II) in place of Co(II) showed only a slight effect on the oxidation (26% conversion) (eq 4).

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(14) After the reaction, most of the NHPI was found to be converted into phthalimide. Treatment of the recovered phthalimide with hydroxylamine gave the NHPI in almost quantitative yield.

(15) To evaluate the extent of decomposition of the resulting adipic acid **3** under the conditions employed, **3** was allowed to react in the presence of NHPI (10 mol %) and Mn(acac)$_2$ (1 mol %) in acetic acid at 100 °C for 10 h. About 90% of **3** was recovered unchanged, and a small amount of **5** (4%) and **6** (1%) was found to be formed.

(16) In the oxidation of cyclohexane using Co(OAc)$_2$ in the presence of aldehyde or cyclohexanone as promoter under oxygen pressure, the Co(III) species formed in situ has been reported to abstract the hydrogen of cyclohexane.[8c,d]

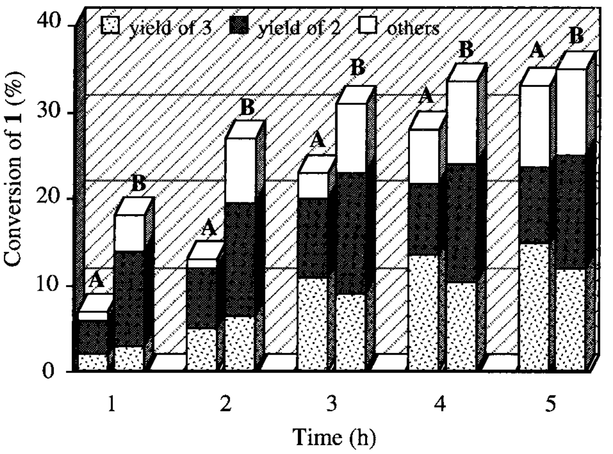


Figure 1. **Time dependence for the oxidation of cyclohexane (1) to cyclohexanone (2) and adipic acid (3) by NHPI/Mn(II) (A) and NHPI/Co(II) (B) system in acetic acid at 100 °C. Conditions: cyclohexane 1 (3 mmol) was allowed to react with oxygen (1 atm) in acetic acid (7.5 mL) at 100 °C in the presence of NHPI (10 mol %) and metal salt (0.5 mol %).**

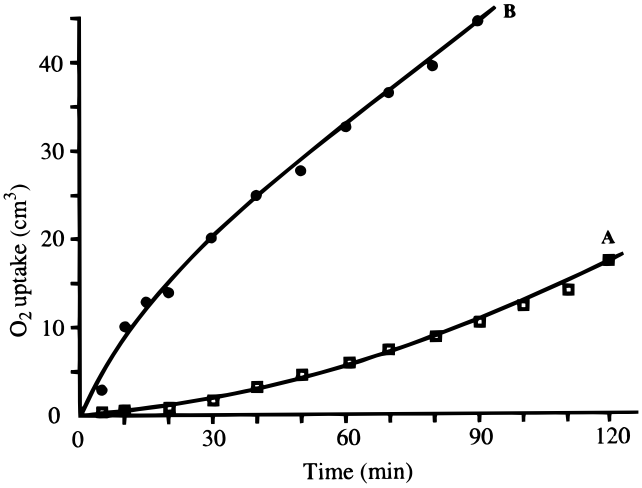
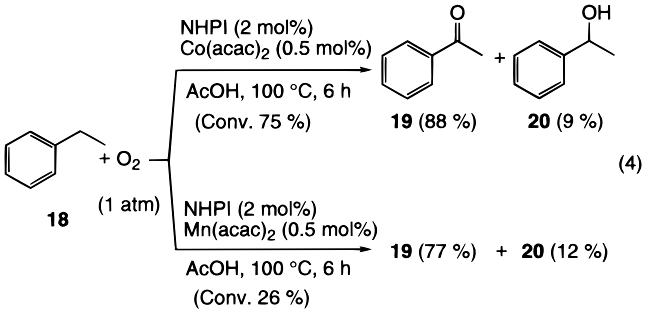


Figure 2. **O_2 uptakes for the oxidation of cyclohexane (1) under atmospheric pressure of oxygen by catalytic systems. Conditions: cyclohexane 1 was allowed to react with oxygen (1 atm) in acetic acid (25 mL) at 80 °C in the presence of (A) NHPI (10 mol %) and Mn(acac)$_2$ (1 mol %), (B) NHPI (10 mol %), Mn(acac)$_2$ (1 mol %), and Co(OAc)$_2$ (0.1 mol %).**



(4)

Table 4. **Oxidation of 1 with molecular oxygen catalyzed by NHPI in the presence of Mn(acac)$_2$ and Co(OAc)$_2$ under various conditions**[a]

run	temp (°C)	convn (%)	selectivity (%) 2	selectivity (%) 3
1	90	50	1	62
2	80	49	1	71
3[b]	80	8	trace	trace
4[c]	80	70	trace	71
5[c,d]	80	58	trace	74
6	70	42	11	72
7[c]	70	60	2	68
8	60	17	48	41

[a] Compound **1** (5 mmol) was allowed to react with oxygen (1 atm) in the presence of NHPI (10 mol %), Co(OAc)$_2$ (0.1 mol %), and Mn(acac)$_2$ (1 mol %) in acetic acid (10 mL) for 14 h. [b] In the absence of NHPI. [c] Reaction was carried out for 24 h. [d] In the absence of Co(OAc)$_2$.

Table 5. **Oxidation of 1 with molecular oxygen catalyzed by NHPI in the presence of Mn(acac)$_2$ and Co(OAc)$_2$ under various conditions**[a]

run	metal (mol %) Co(II)	metal (mol %) Mn(II)	convn (%)	selectivity (%)[b] 2	selectivity (%)[b] 3	selectivity (%)[b] 5
1	0.1	1.0	70	trace	71	9
2	0.05	0.5	63	trace	69	7
3	0.05	0.1	61	1	66	7
4	0.05	0.05	41	34	41	1
5[c,d]	0.05	0.1	60	trace	64	8

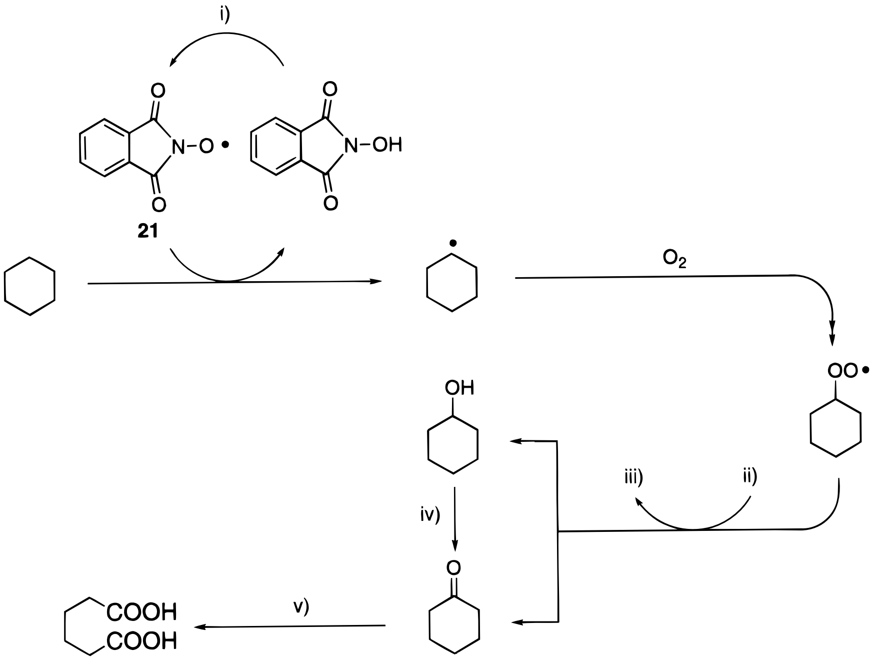
[a] Compound **1** (5 mmol) was allowed to react with oxygen (1 atm) in the presence of NHPI (10 mol %), Co(OAc)$_2$, and Mn(acac)$_2$ in acetic acid (10 mL) at 80 °C for 24 h. [b] Cyclohexanol (**4**), succinic acid (**6**), and cyclohexyl acetate (**7**) were detected as byproducts. [c] Reaction was carried out under air pressure (20 kg/cm^2). [d] Compounds **6** (4%) and **7** (up to 2%) were obtained.

To obtain further information concerning the influence of Co and Mn salts on the reaction rate and selectivity in the NHPI-catalyzed oxidation of **1**, the time-dependence of the conversion of **1** and the selectivity to **2** and **3** by the NHPI/Co(II) system were compared with those by the NHPI/Mn(II) one. The oxidation of **1** by the NHPI/Co(II) proceeded faster than that by the NHPI/Mn(II) at the early stage of the oxidation (Figure 1). However, when a very small amount of Co(II) (0.1 mol %) was added to the NHPI/Mn(II) system, the rapid absorption of O_2 was observed (Figure 2). Since the Co(II) species was found to reduce the induction period of the oxidation of **1** by NHPI/Mn(II), the oxidation of **1** using the NHPI/Mn(II)/Co(II) system was examined (Table 4).

When a very small amount of Co(II) species (0.1 mol %) was added to the NHPI/Mn(II) system, **1** was oxidized at 80 °C to afford **3** in 71% selectivity at 49% conversion after 14 h and in 71% selectivity at 70% conversion after 24 h (runs 2 and 4, Table 4). The oxidation of **1** took place even at 70 °C to form **3** in 68% selectivity (at 60% conversion) (run 7, Table 4). However, the oxidation at 60 °C gave **2** (48%) and **3** (41%) in lower conversion (17%) (run 8, Table 4). The addition of Co(II) species to the NHPI/Mn(II) system in the aerobic oxidation of **1** makes it possible to carry out the oxidation under milder conditions. Thus, the oxidation of **1** by the NHPI/Mn(II)/Co(II) system was investigated in detail (Table 5).

In contrast to the oxidation of **1** by the NHPI/Mn(II) system (run 7, Table 2), the amount of Mn(II) could be reduced from 1 to 0.1 mol % when 0.05 mol % of Co(II) was added to the NHPI/Mn(II) system (run 3, Table 5). Although the selectivity of **1** to **3** was lowered to 41% (at 41% conversion) when the concentration of Mn(II) was

Scheme 1. **A possible reaction path for oxidation of cyclohexane (1) by NHPI/Mn/Co−O_2 system[a]**



[a] (i) O_2 or Co−oxygen complex; (ii) R−H or NHPI; (iii) $R^\bullet$ or **21**; (iv) NHPI−O_2; (v) NHPI/Mn−O_2.

halved from 0.1 to 0.05 mol % (run 4, Table 5), it should be noted that the aerobic oxidation of **1** to **3** by the NHPI/Mn(II) system was significantly accelerated by adding a small amount of Co(II).

It is very important to employ air instead of oxygen as the oxidant to carry out the present oxidation in industrial scale. With this in mind, the aerobic oxidation of **1** using the NHPI/Mn(II)/Co(II) system was examined under 20 kg/cm^2 of air in acetic acid at 80 °C for 24 h. The reaction gave **3** (64%), **5** (8%), and **6** (4%) in 60% conversion (run 5, Table 5).

We have previously reported that phthalimide *N*-oxyl (PINO) (**21**) is a key species in the NHPI-catalyzed aerobic oxidation of hydroaromatic compounds and alkylbenzenes.[10] Similarly, **21** was found to be formed in the NHPI-catalyzed aerobic oxidation of **1** in the presence of a transition metal. When a benzonitrile solution of NHPI and $Co(OAc)_2$ was exposed to oxygen at 80 °C for 10 min, the ESR signal attributed to **21** was observed at $g = 2.0074$, $a_N = 0.43$ mT.[17] However, no ESR signal was obtained when a Co(III) species such as $Co(acac)_3$ was used in place of Co(II) under such conditions. The Co(II) species is known to react with oxygen to form a cobalt−oxygen complex (eq 5).[18] The resulting

$$\begin{aligned} L_2Co(II) + O_2 &\rightleftharpoons L_2Co\text{-}OO^\bullet \\ L_2Co\text{-}OO^\bullet + NHPI &\longrightarrow L_2Co\text{-}OOH + PINO \end{aligned} \qquad (5)$$

cobalt−oxygen complex would accelerate the formation of **21** from the NHPI. For the aerobic oxidation of alkylbenzenes by Co(II)/Mn(II) system, it is reported to be observed the synergistic effect of Co(II) and Mn(II) leading to the reduction of the induction period and the acceleration of the rate in the chain-propagation step.[19] Consequently, the Co salt in the NHPI/Mn/Co system is thought not only to assist the formation of **21** but also to promote the oxidation of **1** by the similar effect of the Co and Mn system reported above.

Scheme 1 shows a proposed reaction pathway for the aerobic oxidation of **1** by the NHPI/Mn(II)/Co(II) system. As **1** was oxidized to **2** and **3** by NHPI alone (runs 2 and 3, Table 1), the *N*-oxyl radical **21** is thought to be the key active species in the present NHPI-catalyzed oxidation of **1**. The Co(II) and Mn(II) species would assist the smooth generation of **21** from NHPI and molecular oxygen and promote the redox degradation of the resulting cyclohexyl hydroperoxide which is eventually converted into adipic acid.

In conclusion, we have developed novel catalytic systems, NHPI/$Mn(acac)_2$ and NHPI /$Mn(acac)_2$/$Co(OAc)_2$, for the direct aerobic oxidation of **1** to **3** under mild conditions. This method, compared with the conventional two-step process which involves aerobic oxidation and nitric acid oxidation, has the following features: (1) the one-step oxidation of **1** to **3** with oxygen or air at lower reaction temperature; (2) high conversion and selectivity to **3**; (3) environmental friendly process not using nitric acid. The present oxidation provides a novel direct method from cyclohexane **1** to adipic acid **3** and would play an important role in industrial organic chemistry.

Experimental Section

^1H and ^{13}C NMR spectra were measured at 270 and 67.5 MHz, respectively, with tetramethylsilane as the internal

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standard. Infrared (IR) spectra were measured using NaCl or KBr pellets. A GC analysis was performed with a flame ionization detector using a 0.2 mm × 25 m capillary column (OV-1). Measurements of oxygen-absorption rates were performed with an isobaric gas-absorption apparatus under a closed-flow system (2 ± 0.1 L of oxygen/h) provided with an electrolyzer. ESR measurements were performed on a JEOL-FE-1X (X-band).

All starting materials and catalysts were purchased from commercial sources and used without further treatment. The yields of products were estimated from the peak areas based on the internal standard technique.

General Procedure for Oxidation of 1. An acetic acid (7.5 mL) solution of **1** (3 mmol), NHPI (49 mg, 10 mol %), and transition metal (0.5 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 100 °C for 6 h. After the solvent was removed under reduced pressure, methanol (25 mL), and a catalytic amount of *concentrated* H_2SO_4 were added to the resulting mixture, and the solution was stirred at 65 °C for 15 h. The resulting solution was extracted with diethyl ether (20 mL × 3). The combined extracts were dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure afforded a clean liquid, which was purified by column chromatography on silica gel (*n*-hexane/AcOEt = 5/1) to give the corresponding oxygenated products.

Compounds **2−7**, **10**, **11, 13, 14, 16,** and **17** were identified through comparison of the isolated products with authentic samples.

Isolation of 3 on a Preparative Scale. An acetic acid (250 mL) solution of **1** (8.4 g, 0.1 mol), NHPI (1.63 g, 10 mol %), and $Mn(acac)_2$ (250 mg, 1 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 100 °C for 20 h. After the solvent was removed under reduced pressure, acetonitrile (100 mL) was added to the reaction mixture to give a white solid. After filtration, 4.62 g of **3** was obtained.

Oxidation of 2. An acetic acid (7.5 mL) solution of **1** (3 mmol), NHPI (49 mg, 10 mol %), and transition metal (0.5 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 100 °C for 6 h. The workup was performed using the same method as previously described.

Preparation of Complex 8. A mixture of **2** (980 mg, 10 mmol), NHPI (408 mg, 2.5 mmol), and $Co(OAc)_2$ (125 mg, 0.5 mmol) in acetic acid (15 mL) was stirred at 100 °C under an oxygen atmosphere for 3 h. Evaporation of solvent under reduced pressure gave a dark-brown solid. The resulting solid was washed with ethyl acetate and dried in vacuo to form complex **8**.

Oxidation of 1 and 2 Catalyzed by NHPI in the Presence of $Co(OAc)_2$ and Complex 8. To a stirred solution of NHPI (49 mg, 10 mol %), $Co(OAc)_2$ (3.7 mg, 0.5 mol %), and complex **8** (10 mg, 4 wt %) in acetic acid (7.5 mL) was added substrate (3 mmol). The mixture was stirred under oxygen atmosphere at 100 °C for 3 h. The workup was performed using the same method as described previously.

Oxidation of 18. An acetic acid (7.5 mL) solution of **18** (3 mmol), NHPI (9.8 mg, 2 mol %), and transition metal (0.5 mol %) was placed in a three-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 100 °C for 6 h. The resulting solution was extracted with diethyl ether (20 mL × 3). The combined extracts were dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure afforded a clean liquid, which was then purified by column chromatography on silica gel (*n*-hexane/AcOEt = 5/1) to give the corresponding oxygenated products, acetophenone (**19**), and 1-phenylethanol (**20**).

Measurements of the Rate of Oxygen Absorption. Measurements of oxygen-absorption rates were performed with an isobaric gas-absorption apparatus under a closed-flow system (2 ± 0.1 L of oxygen/h) provided with an electrolyzer using 25 mL of acetic acid containing cyclohexane (840 mg, 10 mmol), NHPI (163 mg, 10 mol %), $Co(OAc)_2$ (2.5 mg, 0.1 mol %), and $Mn(acac)_2$ (25 mg, 1 mol %) at 80 °C. The oxygen absorption was recorded at regular time intervals.

ESR Measurements. Benzonitrile containing 10^{-2} mmol of NHPI and 5×10^{-4} mmol of $Co(OAc)_2$ was exposed to atmosphere oxygen at 80 °C for 10 min. The air in the ESR tube was replaced by oxygen gas by means of the freeze−pump−thaw method. ESR spectra were obtained under the following conditions: sweep width, 327 ± 2.5 mT; modulation, 0.1 mT; microwave power, 1 mW. The ESR parameter was determined by using solid Mn^{2+} ($g = 2.034$) as a standard.

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