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Oxidation of nitrotoluenes with air using *N*-hydroxyphthalimide analogues as key catalysts

Naoko Sawatari, Satoshi Sakaguchi and Yasutaka Ishii*

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

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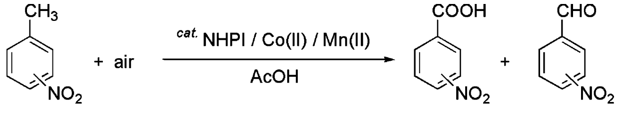
Abstract—Nitrotoluenes are efficiently oxidized with air to the corresponding nitrobenzoic acids by the use of *N*-acetoxyphthalimide (NAPI) as a key catalyst. Thus, *p*- and *m*-nitrotoluenes under 10 atm of air in the presence of NAPI combined with $Co(OAc)_2$ (0.5 mol%) and $Mn(OAc)_2$ (0.05 mol%) at 130°C afforded *p*- and *m*-nitrobenzoic acids in 81 and 92% yields, respectively. *o*-Nitrotoluene was oxidized to *o*-nitrobenzoic acid in 51% yield by the aid of NO_2. © 2003 Elsevier Science Ltd. All rights reserved.

Aerobic oxidations of alkylbenzenes are very important industrial processes for the production of primary and speciality chemicals and monomer materials like terephthalic acid. Nowadays, they are practised in large scale in chemical industry worldwide.[1] These aerobic oxidations are usually carried out under the influence of cobalt salt, manganese salt and bromide ion using acetic acid as a solvent.

However, the aerobic oxidation of nitrotoluenes involving a strong electron-withdrawing substituent to nitrobenzoic acids is very difficult to carry out using this catalytic system even under high pressure of air and higher reaction temperature (around 175°C).[2] Under these conditions, the oxidation is accompanied by undesired side-reactions like decarboxylation of the resulting nitrobenzoic acids and degradation of acetic acid used as a solvent. Other drawbacks of this catalytic system are the use of high corrosive bromide ion and the formation of brominated by-products. To overcome these problems, it is necessary to develop a bromide-free catalytic system for the aerobic oxidations. Although Neuman et al. have reported the Ru-catalyzed liquid-phase oxidation of deactivated toluenes like cyanotoluenes and nitrotoluenes with aqueous sodium hypochloride under phase-transfer conditions,[3] the aerobic oxidation of nitrotoluenes has been little studied by a catalytic system not involving bromide ion. Therefore, the development of an efficient bromide-free catalytic system for the aerobic oxidation of nitrotoluenes is desired for a long time in industrial chemistry. Fortunately, we have recently developed an innovative catalytic method for the aerobic oxidation of hydrocarbons using *N*-hydroxy-phthalimide (NHPI) which serves as a *carbon radical-producing catalyst* (CRPC) from alkanes.[4]

In continuation of our study on the aerobic oxidation of hydrocarbons by this catalytic system, we would like to report the aerobic oxidation of nitrotoluenes, which are very difficult to be oxidized by the conventional autoxidations, by NHPI analogues such as *N*-acetoxyphthalimide (NAPI) and *N*,*N*-dihydroxypyromellitimide (NDHPI) as key catalysts (Eq. (1)).

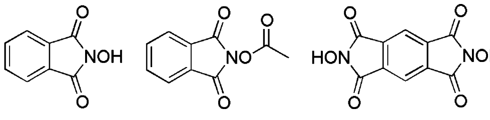


1a-c **2a-c** **3a-c**

a: para-
b: meta-
c: ortho-

(1)

Structural formula



NHPI **NAPI** **NDHPI**

The oxidation of *p*-nitrotoluene (**1a**) with air was examined by the use of several NHPI analogues in acetic acid under various reaction conditions (Table 1).

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* Corresponding author. Tel.: +81-6368-0793; fax: +81-6339-4026; e-mail: ishii@ipcku.kansai-u.ac.jp

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Table 1. Aerobic oxidation of *p*-nitrotoluene (**1a**) by NHPI analogues[a]

Run	Catalyst	Temp. (°C)	Conv. (%)	Yield (%)	
				2a	**3a**
1	NHPI	100	51	43	2
2	NHPI	110	76	65	7
3	NHPI	130	85	78	6
4	–	130	10	nd	nd
5[b]	NHPI	130	74	65	6
6[c]	NHPI	130	33	21	2
7	NAPI	130	91	81	7
8[d]	NDHPI	130	91	80	5

[a] **1a** (2 mmol) was reacted under 10 atm of air in the presence of NHPI analogue (10 mol%), $Co(OAc)_2$ (0.5 mol%) and $Mn(OAc)_2$ (0.05 mol%) in acetic acid (5 mL) for 14 h.
[b] In the absence of $Mn(OAc)_2$.
[c] In the absence of $Co(OAc)_2$.
[d] NDHPI (5 mol%) was used.

The oxidation of **1a** under air (10 atm) in the presence of NHPI (10 mol%), $Co(OAc)_2$ (0.5 mol%) and $Mn(OAc)_2$ (0.05 mol%) at 100°C afforded *p*-nitrobenzoic acid (**2a**) (43%) along with a small amount of *p*-nitrobenzaldehyde (**3a**) (2%) (run 1). The yield of **2a** increased with raising the reaction temperature, and **2a** was obtained in satisfactory yield (78%) at 130°C (run 3). Needless to say, the reaction in the absence of the NHPI under these conditions afforded no nitrobenzoic acid (run 4). Effects of $Co(OAc)_2$ and $Mn(OAc)_2$ on the oxidation of **1a** were examined (runs 5 and 6). The oxidation was markedly retarded without $Co(OAc)_2$, while **1a** was oxidized in relatively good yield (65%) even in the absence of $Mn(OAc)_2$. NHPI analogues, NAPI and NDHPI were also effective for the present oxidation (runs 7 and 8).

In a previous paper, we showed that NAPI, which corresponds to the NHPI protected by the acetyl group, is more stable than the NHPI and that it is gradually hydrolyzed to the NHPI with water containing in acetic acid used as a solvent.[5] In the present oxidation, therefore, the NAPI served as the CRPC to catalyze the oxidation of **1a**. It is interesting to note that NDHPI, involving two hydroxyimide moieties, was efficiently catalyzed the oxidation even in the presence of a half amount (5 mol%) of NHPI which corresponds to 10 mol% of NHPI based on the hydroxyimide unit. This fact indicates that the catalytic activity of hydroxyimide moiety of the NDHPI was comparable to that of the NHPI.

We next examined the oxidation of *m*-nitrotoluene (**1b**) under several conditions in which the **1a** was smoothly oxidized (Table 2).

Table 2. Aerobic oxidation of *m*-nitrotoluene (**1b**) by NHPI analogues[a]

Run	Catalyst	Temp. (°C)	Conv. (%)	Yield (%)	
				2b	**3b**
1	NHPI	130	91	82	6
2	NAPI	130	>99	92	5
3[b]	NDHPI	130	90	80	5
4	NHPI	100	70	62	5

[a] **1b** (2 mmol) was reacted under the same conditions as Table 1.
[b] NDHPI (5 mol%) was used.

The reaction of **1b** by NHPI (10 mol%) combined with $Co(OAc)_2$ (0.5 mol%) and $Mn(OAc)_2$ (0.05 mol%) under 10 atm of air at 130°C gave *m*-nitrobenzoic acid (**2b**) in 82% yield together with *m*-nitrobenzaldehyde (**3b**) (6%) (Table 2, run 1). When NAPI was employed in place of NHPI under these conditions, **1b** was completely converted to form **2b** (92%) and **3b** (5%) (run 2). The oxidation results using 5 mol% of NDHPI were almost the same as those using 10 mol% of NHPI (run 3). The reactivity of **1b** for the aerobic oxidation by NHPI at 100°C was compared with that of **1a** (run 4). It was found that **1b** was oxidized more easily than **1a** to give **2b** in relatively good yield (60%). These results indicate that **1b** is more reactive than **1a**. From the consideration of Hammett constants of **1a** ($\sigma = 0.78$) and **1b** ($\sigma = 0.70$), the reactivity of **1a** and **1b** for the present oxidation seems to be reasonable.

o-Nitrotoluene (**1c**) is known to be reluctant substrate for the aerobic oxidation due to the steric hindrance of the adjacent bulky NO_2 and the electronic effect of NO_2 having the strong electron withdrawing property which deactivates the reactivity of the methyl group. Therefore, it is desired to develop a new efficient method for the oxidation of **1c** through a catalytic process.

Thus, the oxidation of **1c** by CRPC was performed under various reaction conditions (Table 3).

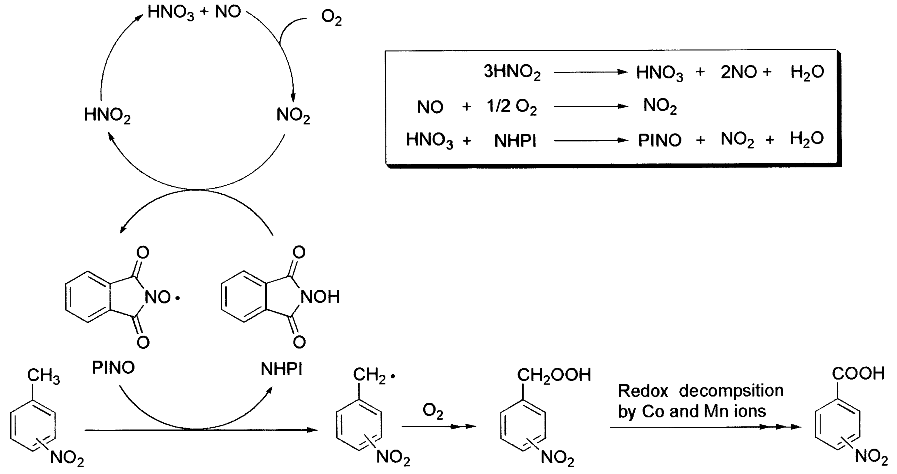
In contrast to the oxidation of **1a** and **1b** by NDHPI and NAPI catalysts which show higher catalytic activities at 130°C, **1c** was difficult to be oxidized by both catalysts at this temperature (runs 1 and 2). By the use of 10 mol% of NDHPI under these conditions, a small amount of *o*-nitrobenzoic acid (2.4%) (**2c**) was formed along with 4% yield of *o*-nitrobenzaldehyde (**3c**) (run 3). These results suggest that the hydrogen abstraction from the methyl group of **1c** is difficult to occur up to 130°C. Thus, the oxidation of **1c** by NHPI assisted by a radical initiator, AIBN, was examined (run 4). It was found that **1c** was oxidized to some extent under the influence of AIBN to give **2c** in 15% yield. Even at higher temperature (150°C), **1c** was difficult to be oxidized by NHPI and NAPI, while NDHPI promoted slightly the oxidation to form **2c** in 16% yield (runs 5–7).

In a previous paper, we reported that the oxidation of methylquinolines by NHPI is markedly accelerated by the addition of a catalytic amount of nitrogen dioxide (NO_2).[6] Thus, the oxidation of **1c** by NHPI/$Co(OAc)_2$/$Mn(OAc)_2$ was run by the addition of NO_2 (20 mol%)

Table 3. Aerobic oxidation of *o*-nitrotoluene (**1c**) by NHPI analogues[a]

Run	Catalyst	Additive (mol%)	Temp. (°C)	Conv. (%)	Yield (%)	
					2c	**3c**
1	NHPI		130	3	nd	nd
2	NAPI		130	8	nd	nd
3[b]	DNHPI		130	17	2.4	4
4	NHPI	AIBN (1)	130	19	15	3
5	NHPI		150	20	11	2
6	NAPI		150	18	10	1
7	NDHPI		150	23	16	3
8	NHPI	NO_2 (20)	150	52	46	4
9	NHPI	AIBN (1)	150	25	11	2
10	NAPI	NO_2 (20)	150	35	29	3
11	NDHPI	NO_2 (20)	150	58	51	4

[a] **1c** (2 mmol) was reacted under the same conditions as Table 1.
[b] NDHPI (5 mol%) was used.



Scheme 1.

at 150°C (run 8). As expected, **1c** was fairly oxidized to give **2c** in 46% yield and **3c** in 4% yield. The same oxidation by adding AIBN instead of NO_2 under these conditions gave **2c** in 11% yield (run 9). However, the yield was not improved by the addition of NO_2 to NAPI for the oxidation of **1c**, probably because of the difficulty of the reaction of the NAPI protected by acetyl group with NO_2 (run 10). In contrast, the yield of **2c** was improved to 51% by adding NO_2 to the NDHPI (run 11).

Similarly, the oxidations of **1a** and **1b** were also accelerated by adding a small amount of NO_2. For example, when the oxidation of **1b** was carried out in the presence of 10 mol% of NO_2 under the reaction conditions as shown in Table 2 run 4, the yield of **2b** increased to 70% at 79% conversion.

It was thought that NO_2, which possesses stronger oxidizing ability than O_2, would smoothly abstract the hydrogen atom from NHPI to form phthalimide *N*-oxyl radical (PINO). The resulting PINO abstracts the hydrogen atom of methyl group of **1c** to form *o*-nitrobenzyl radical which is trapped by O_2 to give benzylperoxy radical followed by **2c** through the redox decomposition of the corresponding hydroperoxide by metal ions (Scheme 1).

The resulting HNO_2 is known to convert into HNO_3 and NO which is readily oxidized to NO_2 under the present conditions.[7] In addition, we show that HNO_3 reacts with the hydroxyimide in the NHPI to form PINO.[8]

In conclusion, the present oxidation of nitrotoluenes with air by the use of CRPC provides an alternative practical green route to nitrobenzoic acids.

Acknowledgements

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