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Synthesis of aromatic aldehydes by aerobic oxidation of hydroaromatic compounds and diarylalkanes using *N*-hydroxyphthalimide (NHPI) as a key catalyst

Yasuhiro Aoki, Satoshi Sakaguchi and Yasutaka Ishii*

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

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Abstract—Aerobic oxidation of hydroaromatic compounds and diarylalkanes by *N*-hydroxyphthalimide (NHPI) under mild conditions afforded the corresponding hydroperoxides in high selectivity. Treatment of the resulting hydroperoxides with sulfuric acid followed by neutralization by a base resulted in phenol and aromatic aldehydes in high selectivity. This method provides a convenient synthetic route to aldehydes involving an aromatic moiety.

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1. Introduction

Aerobic oxidation of alkylbenzenes is an important commercial process for the production of alkyl aromatic hydroperoxides, which are used as oxidants for epoxidation of alkenes like propene as well as raw materials for the production of phenols.¹ The Hock process is well known as a typical method for the concomitant synthesis of phenol and acetone from cumene hydroperoxide obtained by the aerobic oxidation of isopropylbenzene.² Currently, most phenols are manufactured by this method worldwide. Resorcinol and hydroquinone are also prepared by the aerobic oxidation of the *m*- and *p*-diisopropylbenzenes, respectively. However, there is little work reported on the aerobic oxidation of hydroaromatic compounds and diphenyl alkanes to prepare phenols and aldehydes, probably because of the difficulty in carrying out the oxidation selectively.³ In previous papers, we have reported the aerobic oxidation of hydrocarbons catalyzed by NHPI in the presence or absence of transition metals such as cobalt and manganese salts. This oxidation provides a novel efficient catalytic method for the transformation of alkanes to oxygen-containing compounds like alcohols, ketones and carboxylic acids in high conversion and selectivity under mild conditions.⁴ In continuation of our study, the present methodology was extended to the synthesis of various aromatic aldehydes by the aerobic oxidation of hydroaromatic compounds and diphenyl alkanes to hydroperoxides upon treatment with sulfuric acid.

2. Results and discussion

We first examined the aerobic oxidation of tetralin (1) under dioxygen atmosphere (1 atm) in the presence of a catalytic amount of AIBN and NHPI (Eq. 1). Table 1 shows the result for the oxidation of **1** with atmospheric dioxygen catalyzed by NHPI followed by treatment with triphenylphosphine.

Table 1. Oxidation of tetralin (1) with $O_2 \ (1 \ atm)$ by NHPI under various conditions a

Entry	Temperature (°C)	Time (h)	Conv. (%)	Select. (%) ^b	
				3	4
1	75	5	61	80	8
2	65	6	52	87	8
3 ^c	50	6	50	92	4
4 ^d	75	5	22	77	nd
5 ^e	75	5	20	30	nd

^a Compound 1 (2 mmol) was reacted with O_2 (1 atm) in the presence of AIBN (3 mol%) and NHPI (10 mol%) in CH_3CN (5 mL) followed by treatment with PPh₃ (ca. 10 mmol) at room temperature for 2 h.

^b GC yield based on 1 reacted.

^c BPP was used instead of AIBN.

^d In the absence of AIBN.

^e In the absence of NHPI.

Compound 1 was oxidized with O₂ (1 atm) in the presence of AIBN (3 mol%) and NHPI (10 mol%) in acetonitrile at 75 °C for 5 h. The resulting hydroperoxide (2) was treated with excess triphenylphosphine to give 1,2,3,4-tetrahydro-1-naphthol (α -tetralol) (3) and α -tetralone (4) in 80 and 8% selectivity, respectively, at 61% conversion of 1 (entry 1). The same reaction at 65 °C gave almost the same results as

Keywords: Aerobic oxidation; Hydroaromatic compounds; Hock process. * Corresponding author. Tel.: +81 6 6368 0793; fax: +81 6 6339 4026;

e-mail: ishii@ipcku.kansai-u.ac.jp

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that at 75 °C except for a slight decrease of the conversion (entry 2). In order to carry out the reaction at lower temperature, *t*-butyl peroxypivalate (BPP), which decomposes at 55 °C was employed as a radical initiator instead of AIBN. The oxidation can be performed at 50 °C to lead to 3 in high selectivity (92%) along with 4 (4%) at 50% conversion of 1 (entry 3). The reaction of 1 by NHPI alone at 75 °C took place at low conversion (22%) to give 3 (77% selectivity), but the reaction by AIBN in the absence of NHPI resulted in a complex mixture of products (entries 4 and 5). Quite recently, Xu et al. reported the oxidation of 1 with O₂ in the presence of anthraquinones and NHPI at 80 °C to give 4 (88%) and 3 (12%).⁵



In order to obtain further insight into the present reaction, the oxidation was followed by using NHPI/AIBN at 65 °C and using NHPI/BPP at 50 °C, respectively (Fig. 1). The time-conversion curves of **3** and **4** by both systems are similar. The oxidation proceeded smoothly for about 3 h, but it became very slow and was practically terminated



Figure 1. Time-dependence curves for aerobic oxidation of 1 (2 mmol) under O_2 (1 atm): (a) NHPI (10 mol%)/AIBN (3 mol%) in CH₃CN (5 mL) at 65 °C. (b) NHPI (10 mol%)/BPP (3 mol%) in CH₃CN (5 mL) at 50 °C.

after 8 h. This is believed to be due to the decomposition of the NHPI by a side-reaction with a radical species generated from the resulting hydroperoxide **2**. It is known that an increase in the concentration of hydroperoxides causes their steep self-decomposition.

We next tried the conversion of the resulting hydroperoxide **2** into aldehyde by treating with some acids (Table 2).

Table 2. Oxidation of 1 with $O_2 \ (1 \ atm)$ by NHPI followed by treatment with sulfuric $acid^a$

Entry	Temperature (°C)	Time (b)	Conv.	Select. (%) ^b		
	(0)	(11)	(,0)	3	4	5
1	75	3	49	2	4	94
2	75	6	64	3	8	89
3 ^c	75	3	40	<1	7	92
4 ^d	75	3	52	17	46	2
5 ^e	50	3	31	nd	nd	87

^a Compound 1 (2 mmol) was reacted with O₂ (1 atm) in the presence of AIBN (3 mol%) and NHPI (10 mol%) in CH₃CN (5 mL). The reaction mixture was treated with H₂SO₄ (ca. 20 mg) at room temperature for 2 h followed by adding pyridine (ca. 6 mL).

^b GC yield based on 1 reacted.

^c InCl₃·4H₂O (50 mg) was used in place of H₂SO₄.

^d CeCl₃·7H₂O (50 mg) was used in place of H₂SO₄.

^e BPP (3 mol%) was used in place of AIBN.

The oxidation of 1 in the presence of AIBN and NHPI at 75 °C for 3 h followed by treatment with sulfuric acid at room temperature afforded 3-(2-hydroxyphenyl)butanal (5) (94%), **4** (4%), and **3** (2%) at 49% conversion of **1** (entry 1). When the reaction was prolonged to 6 h, the conversion was increased to 64% but the selectivity to 5 was slightly decreased (entry 2). Treatment of 2 with a Lewis acid like InCl₃, which does not decompose in aqueous medium, gave almost the same result as that of sulfuric acid (entry 3). However, when CeCl₃ was employed instead of InCl₃, tetralone 4(46%) was formed as the principal product along with tetralol 3(17%), but the desired 5 was formed in only 2% yield (entry 4). This shows that CeCl₃ serves as a metal ion, which promotes the redox decomposition of the hydroperoxide 2. The reaction using BPP instead of AIBN at 50 °C led to 5 in 87% selectivity at 31% conversion of 1 (entry 5).

On the basis of these results, we examined the synthesis of aldehydes having an aromatic moiety from several hydroaromatic compounds and diphenyl alkanes (Table 3).

Indane (6) was reacted under the same conditions as entry 1 in Table 2 to afford 3-(2-hydroxyphenyl)propanal (8) (81%) and indanone (7) (10%) at 42% conversion of 6 (entry 1). In this reaction, a trace amount of 1-indanol was formed. *sym*-Octahydroanthracene (9) was easily oxidized under these conditions to give 1,2,3,4,6,7,8,9-octahydroanthracen-1-one (10) (13%) and 4-(5,6,7,8-tetrahydro-3-hydroxy-2naphthyl)butanal (11) (73%) at higher conversion (85%) (entry 2). In this oxidation, however, no products in which both cyclohexyl rings in 9 are oxidized were obtained. It was found that diphenyl methane (12) was less reactive than 1. Hence, benzonitrile, which is capable of raising the

Table 3. Conversion of hydroaromatic compounds and diphenyl alkanes into aldehydes^a

Entry	Substrate	Temperature (°C)/Time (h) (Solvent)	Conv. (%)	Product (select. (%)) ^b	
1		75/3 (CH ₃ CN)	42	0 7 (10)	ОН ОН 8 (81)
2	y 9	75/3 (CH ₃ CN)	85	0 10 (13)	OH 0 11 (73)
3	Ph Ph 12	100/5 (PhCN)	30	O Ph H 13 (98)	PhOH 14 (99)
4	Ph Ph 15	100/3 (PhCN)	37	Ph H O 16 (97)	14 (62)
5	15	75/3 (CH ₃ CN)	23	16 (96)	14 (83)
6 ^c	15	50/18 (CH ₃ CN)	33	16 (99)	14 (97)
7 ^c	Ph Ph 17	50/3 (CH ₃ CN)	24	O Ph 18 (>99)	14 (67)

^a Substrate (2 mmol) was reacted under the same conditions as entry 1 in Table 2.

^b GC yield based on substrate reacted.

^c BPP (*t*-butyl peroxypivalate) was used instead of AIBN.

reaction temperature to 100 °C, was used as a solvent. The reaction gave benzaldehyde (13) and phenol (14) in excellent selectivity at moderate conversion of 12 (entry 3). 1,2-Diphenylethane (15) reacted in the same way as 12 to give the corresponding aldehyde, phenylacetaldehyde (16), in high selectivity (97%) at 37% conversion (entry 4). Although long reaction time is needed for the oxidation of 15 at lower temperature (75 or 50 °C), 15 was found to be slowly oxidized even at 50 °C to give 16 in high selectivity (entry 6). However, oxidation of 1,1-diphenylethane (17) having a methine group more easily proceeded than that of 15 to give acetophenone (18) in high selectivity (99%) at 24% conversion (entry 7).

In conclusion, we have developed a method for aerobic oxidation of hydroaromatic compounds and diarylalkanes to the corresponding hydroperoxides selectively. Further treatment of the resulting hydroperoxides with sulfuric acid followed by neutralization with a base produced phenol derivatives and aromatic aldehydes in high selectivity. This method provides a convenient synthetic route to aldehydes involving an aromatic group.

3. Experimental

3.1. General procedure

¹H and ¹³C NMR were measured at 270 and 67.5 MHz, respectively, in CDCl₃ with TMS as the internal standard. Infrared (IR) spectra were measured as thin films on NaCl

plate or KBr press disk. A GLC analysis was performed with a flame ionization detector using a $0.2 \text{ mm} \times 25 \text{ m}$ capillary column (OV-17). Mass spectra were determined at an ionizing voltage of 70 eV. All starting materials, catalysts, and initiators 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.

3.2. General procedure for the oxidation of tetralin (1) to 1,2,3,4-tetrahydro-1-naphthol (α -tetralol) (3) and α -tetralone (4)

An acetonitrile (5 mL) solution of tetralin (1) (2 mmol), AIBN (3 mol%), and NHPI (10 mol%) was placed in a twonecked flask equipped with a balloon filled with O_2 at 50–75 °C for 5–6 h. The reaction mixture was treated with an excess amount of PPh₃ at 25 °C for 2 h.

3.3. General procedure for the oxidation of various substrates to aldehyde and ketone derivatives

An acetonitrile (5 mL) solution of substrate (2 mmol), AIBN (3 mol%), and NHPI (10 mol%) was placed in a twonecked flask equipped with a balloon filled with O_2 at 75 °C for 3 h. The reaction mixture was treated with H_2SO_4 (ca. 20 mg) in CH₃CN (1 mL) at 25 °C for 2 h. The mixture was neutralized by adding pyridine (ca. 6 mL). The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (*n*-hexane/ AcOEt = 10:1) to give aldehydes and ketones. Products were characterized by ¹H and ¹³C NMR, IR, and GC–MS.

3.3.1. 4-(2-Hydroxyphenyl)butanal (5).⁶ ¹H NMR δ 9.79 (s, 1H), 7.09–6.79 (m, 4H), 5.66 (br, 1H), 2.62 (t, J=7.2 Hz, 2H), 2.55 (t, J=6.7 Hz, 2H), 1.95–1.90 (m, 2H); ¹³C NMR δ 203, 130, 127, 120, 115, 42.9, 29.3, 22.1; IR (NaCl) 3420, 3066, 3034, 2937, 2723, 1716, 1593, 1503, 1454, 1231, 1175, 1107, 755 cm⁻¹; MS m/e=40, 51, 65, 77, 91, 107, 120, 133, 145, 164.

3.3.2. 1,2,3,4,6,7,8,9-Octahydroanthracen-1-one (**10**).⁷ ¹H NMR δ 7.74 (s, 1H), 7.26 (s, 1H), 2.87 (t, *J*=6.2 Hz, 2H), 2.77 (t, *J*=6.4 Hz, 4H), 2.60 (t, *J*=6.4 Hz, 2H), 2.09 (q, *J*=6.2 Hz, 4H); ¹³C NMR δ 198, 152, 143, 141, 135, 129, 128, 75; 53, 39, 29, 23; IR (NaCl) 2934, 2850, 1727, 1727, 1679, 1436, 1265, 1041, 894, 747 cm⁻¹; MS *m/e* = 40, 51, 63, 77, 91, 103, 115, 129, 144, 158, 172, 185, 200; HRMS (EI, M⁺) calcd for C₁₄H₁₆O: 200.1201, found: 200.1204.

3.3.3. 4-(5,6,7,8-Tetrahydro-3-hydroxy-2-naphthyl)butanal (**11**). ¹H NMR δ 9.74 (s, 1H), 6.75 ppm (s, 1H), 6.48 (s, 1H), 2.63–2.48 (m, 8H), 1.89 (m, *J*=6.8 Hz, 2H), 1.70 (m, *J*=7.3 Hz, 4H), ¹³C NMR δ 204, 152, 136, 131, 128, 124, 115, 43, 29, 28, 23, 22; IR (NaCl) 3412, 3004, 2927, 2855, 1712, 1620, 1517, 1424, 1247, 1191, 1094, 918, 858, 777 cm⁻¹; MS *m*/*e*=40, 55, 65, 77, 91, 105, 115, 133, 146, 161, 174, 187, 200, 218; HRMS (EI, M⁺) calcd for C₁₄H₁₈O₂: 218.1307, found: 218.1332.

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