



## N-Hydroxyphthalimide in combination with Cu(II), Co(II) or Mn(II) salts as catalytic systems for the oxidation of isopropyl-aromatic hydrocarbons with oxygen

Beata Orlińska\*

Department of Chemical Organic Technology and Petrochemistry, Silesian University of Technology, Krzywoustego 4, Gliwice 44-100, Poland

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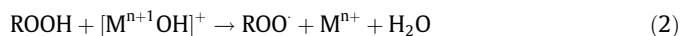
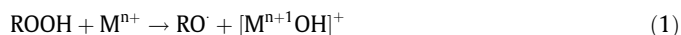
### ABSTRACT

Catalytic systems consisting of *N*-hydroxyphthalimide in combination with copper(II), cobalt(II) and manganese(II) acetylacetonate, acetate or chloride were applied to the oxidation of cumene with oxygen. The use of these catalytic systems decreases cumyl hydroperoxide selectivity as a result of the decomposition reaction of hydroperoxide to 2-phenyl-2-propanol and acetophenone. It has been demonstrated that the use of *N*-hydroxyphthalimide in combination with copper salts at 60 °C results in high alcohol content whereas ketone is the major product at 90 °C. The results can be used to develop a method for alcohol or ketone synthesis from other isopropyl-aromatic hydrocarbons.

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The oxidation of isopropyl-aromatic hydrocarbons to hydroperoxides is one of the several steps in the industrial synthesis of phenols and acetone. Every year, more than 7 million tonnes of phenol are produced from cumene,<sup>1</sup> and analogous industry-scale syntheses have been developed for the production of hydroquinone, resorcinol, cresols and 2-naphthol.<sup>2</sup> Several contemporary studies have investigated the application of these methods to the production of other hydroxyaromatics, including 2,6-dihydroxynaphthalene and 4,4'-dihydroxybiphenyl, used for the synthesis of liquid crystals and high performance polyesters.<sup>3,4</sup>

The liquid phase oxidation of isopropyl-aromatic hydrocarbons proceeds according to a widely known free radical chain mechanism.<sup>5,6</sup> Transition metal salts, such as Cu(I)/Cu(II), Co(II)/(III) and Mn(II)/(III), are typically used as catalysts in these oxidation processes,<sup>6,7</sup> wherein their catalytic effect lowers the activation energy of the decomposition reaction of the hydroperoxide (reactions 1 and 2).

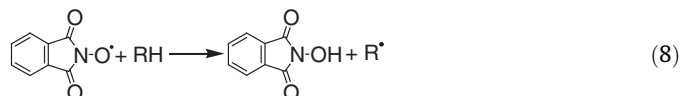
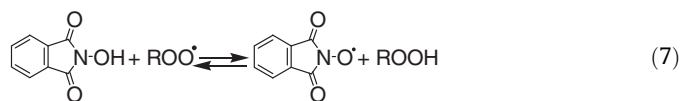
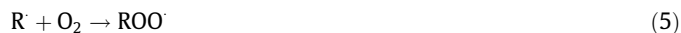


The radicals formed by hydroperoxide decomposition initiate subsequent chains of reactions that increase the reaction rate and decrease the hydroperoxide selectivity; hence the oxidation products contain more alcohol and ketone due to hydrogen abstraction and  $\beta$ -scission of alkoxy radicals (reactions 3 and 4).



R = 1-methyl-1-arylethyl group; R' = aryl group.

Recently, *N*-hydroxyphthalimide (NHPI) has been demonstrated to be a free radical oxidation catalyst.<sup>8–13</sup> In contrast to transition metals, NHPI does not accelerate the hydroperoxide decomposition reaction. The catalytic activity of NHPI results from phthalimide-*N*-oxyl radical (PINO) formation in the propagation step of the oxidation process (reactions 5–8).<sup>13–17</sup> It was observed that PINO radicals abstract H-atoms much faster than peroxy radicals.<sup>18,19</sup>



The catalytic activity of NHPI has been demonstrated in several processes, including cumene,<sup>4,8,10,12</sup> 2,6-diisopropyl-naphthalene,<sup>3,4,11,12</sup> 4,4'-diisopropylbiphenyl<sup>4,12</sup> and 1,3,5-triisopropylbenzene<sup>20</sup> oxidations. High yields (>70%) and hydroperoxide

\* Tel.: +48 32 2372791; fax: +48 32 2371032.

E-mail address: beata.orlinska@polsl.pl.

selectivities were obtained when cumene,<sup>10</sup> 2,6-diisopropyl-naphthalene<sup>3</sup> or 1,3,5-triisopropylbenzene<sup>20</sup> were oxidised in the presence of NHPI (10 mol %) at 75 °C using acetonitrile as the solvent.

Isopropyl-aromatic hydrocarbon oxidation using a catalyst consisting of NHPI and a cobalt(II) salt has also been reported in the literature, wherein high yields of alcohols or ketones were obtained depending on the reaction conditions. If 2,6-diisopropyl-naphthalene and 4,4'-diisopropylbiphenyl are oxidised in the presence of NHPI and a Co(II) salt at 40 °C using acetonitrile as the solvent, the diols 2,6-di(1-hydroxy-1-methylethyl)naphthalene and 4,4'-di(1-hydroxy-1-methylethyl)biphenyl, in yields of approximately 90%, were obtained.<sup>4,12</sup> When the same catalyst was used for the oxidation of 2,6-diisopropyl-naphthalene at 75 °C for 15 h, 2-acetyl-6-isopropyl-naphthalene was obtained in a yield of 31%.<sup>21</sup>

Therefore, NHPI in combination with metal salts can be used in the processes where alcohols or ketones are the desired products.

In this Letter, we report the influence of several catalysts consisting of NHPI and different variable valence metal salts for the oxidation of cumene, as a model compound. The purpose of this investigation was to evaluate the influence of the aforementioned catalysts on the resultant product composition to evaluate the feasibility of synthesising alcohols or ketones from isopropyl-aromatics. Previous studies have indicated that the type of metal salt used can influence the composition of the resulting products.<sup>6,7,22</sup>

Thus, cumene was oxidised in the presence of NHPI in combination with copper(II), manganese(II) or cobalt(II), acetylacetonate, acetate or chloride. Similarly, oxidation reactions in the presence of NHPI or Cu(acac)<sub>2</sub> were also carried out for comparison. These oxidations were carried out using acetonitrile or benzonitrile as solvents because of the low solubility of NHPI in non-polar hydrocarbons, and furthermore, all the metal salts used in this study were soluble in these solvents. The obtained cumene conversions

and hydroperoxide, acetophenone and 2-phenyl-2-propanol selectivities are presented in Table 1.

According to the literature, the use of NHPI as a catalyst significantly increases cumene conversion, while maintaining a high cumyl hydroperoxide selectivity (entries 9 and 11). In contrast, the use of a catalytic system consisting of NHPI and a metal salt decreases hydroperoxide selectivity in most processes as a result of the decomposition of hydroperoxide to acetophenone and 2-phenyl-2-propanol. It has been observed that the type of metal salt used in combination with NHPI affects the cumene conversion and product composition.

In the presence of an NHPI and a metal salt catalyst, the resultant cumene conversions decrease in the order of acetylacetonate > acetate > chloride. Here, the chloride anion influences the oxidation process negatively, as lower conversion rates were obtained independently from the activities of the chlorides in the hydroperoxide decomposition.

Among the various metals used in these catalytic systems, copper exhibited the highest activity in hydroperoxide decomposition even at low temperature.

It has been also observed that the type of metal salt used affects the molar ratio of acetophenone to 2-phenyl-2-propanol in oxidation products. This ratio was higher in the presence of copper ions, lower in the presence of cobalt ions and increased in the order acetylacetonate < acetate < chloride. For example, in the presence of NHPI and Co(acac)<sub>2</sub>, Cu(acac)<sub>2</sub> and CuCl<sub>2</sub> at 70 °C this ratio reached values of 0.47, 0.63 and 1.2, respectively.

The different behaviours of the metal ions may be a result of their different redox potentials and, in association with this, their different behaviours in catalysing hydroperoxide decomposition.<sup>6,7</sup> In contrast to cobalt ions, which reduce and oxidise hydroperoxides into alkoxy and alkylperoxy radicals, copper ions only reduce hydroperoxides into alkoxy radicals, but a catalytic process is possible since there are several routes available for regenerating Cu(I),

**Table 1**  
Cumene oxidation with oxygen in the presence of NHPI and Cu(II), Co(II) or Mn(II) salts<sup>a</sup>

Entry	Catalyst	Time (h)	Temp. (°C)	Conv. (mol %)	Selectivity (mol %)		
					Cumyl hydroperoxide	Acetophenone	2-Phenyl-2-propanol
1	NHPI/CuCl <sub>2</sub> ·2H <sub>2</sub> O	3	50	50	20	29	50
2	NHPI	3	60	53	100	0	0
3	NHPI	5	60	68	100	0	0
4	NHPI/Cu(acac) <sub>2</sub>	3	60	68	44	10	45
5	NHPI/Cu(acac) <sub>2</sub>	4.5	60	72	19	15	63
6	NHPI/CuCl <sub>2</sub> ·2H <sub>2</sub> O	3	60	57	12	37	47
7	NHPI/Co(acac) <sub>2</sub>	3	60	56	94	0	4
8	NHPI/Co(acac) <sub>2</sub>	5.5	60	75	60	6	33
9	—	3	70	6	100	0	0
10	Cu(acac) <sub>2</sub>	3	70	12	9	—	—
11	NHPI	3	70	53	100	0	0
12	NHPI/Cu(acac) <sub>2</sub>	3	70	55	26	27	43
13	NHPI/Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O	3	70	52	23	32	45
14	NHPI/CuCl <sub>2</sub> ·2H <sub>2</sub> O	3	70	47	10	46	40
15	NHPI/Co(acac) <sub>2</sub>	3	70	51	16	27	57
16	NHPI/Co(OAc) <sub>2</sub> ·4H <sub>2</sub> O	3	70	41	21	31	52
17	NHPI/CoCl <sub>2</sub> ·6H <sub>2</sub> O	3	70	41	100	0	0
18	NHPI/Mn(acac) <sub>2</sub>	3	70	52	82	6	13
19	NHPI/Mn(OAc) <sub>2</sub> ·4H <sub>2</sub> O	3	70	48	100	0	0
20	NHPI/MnCl <sub>2</sub> ·4H <sub>2</sub> O	3	70	32	100	0	0
21	NHPI	3	90	40	91	—	—
22	NHPI/Cu(acac) <sub>2</sub>	3	90	29	4	57	26
23	NHPI/CuCl <sub>2</sub> ·2H <sub>2</sub> O	3	90	29	6	58	26

<sup>a</sup> Cumene (1.4 mL; 10 mmol), 10 mL of solvent (acetonitrile at 50–70 °C or benzonitrile at 90 °C), initiator (3 mol %) (2,2'-azobis(2-methylpropionitrile) at 50–70 °C or 1,1'-azobis(cyclohexanecarbonitrile) at 90 °C), NHPI (10 mol %, 0.163 g) and metal salt (0.5 mol %) were placed in a 25 mL two-necked flask of a gasometric apparatus supplied with a magnetic stirrer (1000 rpm), heating bath and gas burette filled with oxygen. The amount of consumed oxygen was measured over the course of 3 h and used to calculate conversion. The amount of cumyl hydroperoxide was iodometrically determined according to the described method,<sup>28</sup> and the amount of acetophenone and 2-phenyl-2-propanol was determined using HPLC using a Waters Alliance 2690 HPLC equipped with an autosampler, UV detector (Waters photodiode array), and Nova-Pak Silica column (60 Å, 4 μm, 150 × 3.9 mm; Waters). A mixture of hexane and 2-propanol 99/1 was used as the mobile phase (flow 1 mL/min); 2-phenyl-2-propanol was detected at 210 nm and acetophenone at 240 nm using an external standard.<sup>29</sup>

including oxidation of alkyl radicals.<sup>7</sup> The redox potential can also be influenced by ligand type, which can explain the different observed behaviours of the various salts.<sup>6</sup>

The influence of temperature on cumene oxidation in the presence of NHPI and the aforementioned metal salts was investigated in the temperature range 50–90 °C. At 50 °C, long induction periods were observed (approximately 40 min). When the reaction temperature was increased from 60 to 90 °C, cumene conversion decreased. At 90 °C, oxidation processes were quickly inhibited. This observed quenching of cumene conversion is most likely caused by thermal decomposition of NHPI,<sup>4</sup> as well as by an increased number of reactions that inhibit the process. It is assumed that phenol, a free radical process inhibitor, can be formed by the acid rearrangement of cumene hydroperoxide. These acids (e.g., formic acid) can be obtained from the oxidation of the methyl radical formed during  $\beta$ -scission of the 1-methyl-1-phenylethoxy radical into acetophenone. Therefore, acetophenone formation can be connected to acid formation and process inhibition. It has been established that a rise in temperature leads to increased  $\beta$ -scission of alkoxy radicals to the ketone.<sup>23–25</sup> In our studies this tendency was confirmed. For example, the ketone to alcohol ratio in cumene oxidation products obtained in the presence of NHPI/CuCl<sub>2</sub>·2H<sub>2</sub>O reached values of 0.6 and 2.2 at 50 °C and 90 °C, respectively.

The results presented herein for cumene oxidation could be used to develop a method for alcohol or ketone synthesis from other isopropyl-aromatics. It has been demonstrated that the use of NHPI in combination with copper salts at 60 °C results in high alcohol amount whereas ketone is the major product at 90 °C. Unfortunately, it was observed that temperature increases beyond a certain point decrease the cumene conversion, which might limit the direct synthesis of ketones from isopropyl-aromatics.

We next intend to investigate the oxidations of 2-isopropyl-naphthalene, *p*-isopropylanisole, 2,6-diisopropyl-naphthalene, 4,4'-diisopropylbiphenyl and 2-methoxy-6-isopropyl-naphthalene in the presence of an NHPI/copper salt catalyst. Alcohols and ketones obtained by this method can be used in the production of valuable products (fragrances, e.g., 2-acetylnaphthalene,<sup>26</sup> pharmaceuticals, e.g., 4-methoxyacetophenone,<sup>27</sup> polyesters and liquid crystals<sup>21</sup>).

This Letter reports a catalytic system composed of a copper salt and NHPI which has been rarely used previously. Among isopro-

pyl-aromatics, only oxidation of 1,3,5-triisopropylbenzene in the presence of Cu(OAc)<sub>2</sub>/NHPI was described and this resulted in a complex mixture.<sup>20</sup>

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## References and notes

- Schmidt, R. J. *Appl. Catal. A: Gen.* **2005**, *280*, 89.
- Weissermel, K.; Arpe, H. J. *Industrial Organic Chemistry*; VCH Verlagsgesellschaft mbH: Weinheim, 1993. pp 324, 349–357, 358–362.
- Aoki, Y.; Sakaguchi, S.; Ishii, Y. *Adv. Synth. Catal.* **2004**, *346*, 199–202.
- Minisci, F.; Recupero, F.; Cecchetto, A.; Gambarotti, C.; Punta, C.; Paganelli, R. *Org. Process Res. Dev.* **2004**, *8*, 163–168.
- Howard, J. A. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 2, p 3.
- Denisov, E. T.; Afanas'ev, I. B. *Oxidation and Antioxidants in Organic Chemistry and Biology*; Taylor & Francis Group: Boca Raton, 2005. pp 23–72, 359–382.
- Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981. pp 18–25, 38–41.
- Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T.; Nishiyama, Y. *J. Org. Chem.* **1995**, *60*, 3934–3935.
- Ishii, Y.; Sakaguchi, S.; Iwahama, T. *Adv. Synth. Catal.* **2001**, *343*, 393–427.
- Fukuda, O.; Sakaguchi, S.; Ishii, Y. *Adv. Synth. Catal.* **2001**, *343*, 809–813.
- Ishii, Y.; Sakaguchi, S. *Catal. Today* **2006**, *117*, 105–113.
- Minisci, F.; Punta, C.; Recupero, F. *J. Mol. Catal. A: Chem.* **2006**, *251*, 129–149.
- Recupero, F.; Punta, C. *Chem. Rev.* **2007**, *107*, 3800–3842.
- Amorati, R.; Lucarini, M.; Mugnaini, V.; Pedulli, G. F. *J. Org. Chem.* **2003**, *68*, 1747–1754.
- Sheldon, R. A.; Arends, I. W. J. *Mol. Catal. A: Chem.* **2006**, *251*, 200–214.
- da Silva, G.; Bozzelli, J. W. *J. Phys. Chem. C* **2007**, *111*, 5760–5765.
- Hermans, I.; Vereecken, L.; Jacobs, P.; Peeters, J. *Chem. Commun.* **2004**, 1140–1141.
- Hermans, I.; Jacobs, P.; Peeters, J. *Phys. Chem. Chem. Phys.* **2007**, *9*, 686–690.
- Hermans, I.; Peeters, J.; Jacobs, P. *Top. Catal.* **2008**, *50*, 124–132.
- Aoki, Y.; Hirai, N.; Sakaguchi, S.; Ishii, Y. *Tetrahedron* **2005**, *61*, 10995–10999.
- Nakamura, R.; Obora, Y.; Ishii, Y. *Tetrahedron* **2009**, *65*, 3577–3581.
- Orlińska, B.; Zawadiak, J.; Gilner, D. *Appl. Catal. A: Gen.* **2005**, *287*, 68–74.
- Walling, C.; Wagner, P. J. *J. Am. Chem. Soc.* **1964**, *86*, 3368–3375.
- Walling, C.; Padwa, A. *J. Am. Chem. Soc.* **1963**, *85*, 1593–1597.
- Avila, D. V.; Brown, C. E.; Ingold, K. U.; Luszytyk, J. *J. Am. Chem. Soc.* **1993**, *115*, 466–470.
- Guenin, E.; Boudot, P.; Sillon, P.; Vincenti, P.; Taylor, C.; Durand, P. WO Patent 9944575, 1999; *Chem. Abstr.* **1999**, *131*, 219034.
- Pei, Y.; Tede, H. U.S. Patent 5,208,343, 1993; *Chem. Abstr.* **1993**, *119*, 160124.
- Zawadiak, J.; Gilner, D.; Kulicki, Z.; Baj, S. *Analyst* **1993**, *118*, 1081.
- Baj, S.; Kulicki, Z. *J. Chromatogr.* **1991**, *588*, 33–39.