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Metal-Free: An Efficient and Selective Catalytic Aerobic Oxidation of Hydrocarbons with Oxime and *N*-Hydroxyphthalimide

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Abstract: A non-metal catalytic system consisting of dimethylglyoxime (DMG) and *N*-hydroxyphthalimide (NHPI) for the selective oxidation of hydrocarbons with dioxygen is described. The synergistic effect of DMG and NHPI ensures its efficient catalytic ability: 82.1% conversion of ethylbenzene with 94.9% selectivity for acetophenone could be obtained at 80 °C under 0.3 MPa of dioxygen in 10 h. Several hydrocarbons were efficiently oxidized to their corresponding oxygenated products under mild conditions.

Keywords: aerobic oxidation; catalyst design; dimethylglyoxime; hydrocarbons; *N*-hydroxyphthalimide

Introduction

The selective catalytic oxidation of hydrocarbons, such as ethylbenzene, cyclohexane, *p*-xylene and toluene, with molecular oxygen is a primary and essential tool for organic synthesis and industrial chemistry.[1] For this purpose, many efficient catalysts containing transition metals have been reported.[2] Although these catalyst systems could improve the oxidation of hydrocarbons, the disadvantages of metallic toxicity and the high expense could not be avoided. Yet improving the catalytic performance of such aerobic oxidations remains an industrial and scientific challenge because of increasing energy costs and growing environmental concerns. In recent years, *N*-hydroxyphthalimide (NHPI) has been used as a valuable catalyst for the efficient aerobic oxidation of various organic compounds under mild reaction conditions in the presence of some metallic compounds.[3] Interestingly, some non-metallic compounds, such as α,α-azoisobutyronitrile,[4] aldehydes,[5] anthraquinones,[6] xanthone/tetramethylammonium chloride,[7] acridine yellow/Br_2,[8] and quaternary ammonium bromides,[9] can accelerate the NHPI-based oxidation. Herein we report that an oxime, especially the inexpensive dimethylglyoxime (DMG), in combination with NHPI, serves as a metal-free catalytic system for the aerobic oxidation of hydrocarbons which provides an unprecedented and efficient catalytic method for the transformation of hydrocarbons to their oxygen-containing compounds under moderate conditions.

Results and Discussion

Catalytic Activity of Various Oximes in the Presence of NHPI

The catalytic properties of various oximes were examined in the aerobic oxidation of ethylbenzene at 80 °C under 0.3 MPa O_2 for 6 h. The oxidation results are listed in Table 1. It was found that 10 mol% acetaldoxime in combination with 10 mol% NHPI realized 43.9% conversion of ethylbenzene with the selectivities of 59.4% for acetophenone (AcPO), 16.5% for 1-phenylethanol (PEA) and 24.1% for 1-phenylethyl

Table 1. Oxidation of ethylbenzene catalyzed by different oximes and NHPI.[a]

Entry	Catalyst	Conversion [%]	Selectivity [%]		
			AcPO	PEA	PEHP
1	acetaldoxime/NHPI	43.9	59.4	16.5	24.1
2	acetoxime/NHPI	50.3	56.5	14.8	28.7
3	cyclohexanone oxime/NHPI	45.7	51.7	15.6	32.7
4	DMG/NHPI	74.5	74.9	17.4	7.7
5	DMG	trace	–	–	–
6	NHPI	23.2	54.8	12.0	33.2

[a] *Reaction conditions:* 16 mmol ethylbenzene, 10 mol% oxime, 10 mol% NHPI, 10 mL CH_3CN, 0.3 MPa O_2, 80 °C, 6 h.

hydroperoxide (PEHP) (Table 1, entry 1). And acetoxime/NHPI and cyclohexanoneoxime/NHPI gave 50.3% and 45.7% conversions, respectively (entries 2 and 3). To our delight, by using 10 mol% DMG and 10 mol% NHPI together, the conversion of ethylbenzene increased to 74.5%, and the selectivity of AcPO also increased to 74.9% (entry 4). GC and GC-MS measurements indicated that the products in all oxidations were AcPO, PEA and PEHP without any appreciable benzoic acid, the overoxidation product. In sharp contrast, the oxidation could not occur by using DMG alone (entry 5). And in the absence of DMG, NHPI realized only 23.2% conversion (entry 6), which was in accordance with the result in the previous literature.[11] Therefore, it clearly showed that the combination of oximes and NHPI, DMG and NHPI in particular, could significantly promote the aerobic oxidation of ethylbenzene due to their synergistic effect.

It had been reported that several organic compounds could mediate the NHPI-based oxidation. Among these mediators, α,α-azoisobutyronitrile[4] and aldehydes[5] play the sole role of a radical initiator to induce the formation of phthalimide *N*-oxyl radical (PINO), and they are consumed during the reactions and are not recoverable. Noticeablely, purely organic substituted anthraquinones,[6] the couple of xanthone and tetramethylammonium chloride,[7] and the couple of acridine yellow and Br_2[8] can work as the cocatalytic components for the NHPI-based oxidation. By comparison, the simple and inexpensive DMG/NHPI exhibits nearly the same catalytic activity as the catalytic systems mentioned above, and avoids the corrosive component.

Influence of Reaction Conditions on Ethylbenzene Oxidation Catalyzed by DMG/NHPI

Due to the poor solubility of NHPI in organic solvents, the NHPI-catalyzed aerobic oxidation was often conducted in polar solvents such as acetonitrile or acetic acid. In our tests using 10 mol% NHPI and 10 mol% DMG, the ethylbenzene (16 mmol) oxidation at 80 °C under 0.3 MPa O_2 for 6 h in 10 mL dichloromethane and tetrachloromethane solution gave rather low conversions of 20.6% and 15.7%, respectively. On the other hand, in polar solvents such as acetonitrile, acetic acid, trifluoroacetic acid and tetrahydrofuran, the conversions reached 74.5%, 44.9%, 40.7% and 67.3%, respectively. Therefore, acetonitrile seems the superior choice over the other solvents screened.

The catalytic performances of DMG/NHPI in acetonitrile were examined in detail as shown in the following paragraphs. Table 2 displays the oxidation results using different catalyst amounts. In comparison with the oxidation using 10 mol% NHPI and 10 mol% DMG (Table 2, entry 1), the conversion of ethylbenzene markedly decreased when the amounts of both the catalytic components were contracted to 5 mol% (entry 2). With the amount of one component decreased to 5 mol%, the conversions still remained low in spite of increasing the amount of the other component to 15 mol% (entries 3–6). On the other hand, when the amounts of either one component or both the components were increased to 15 mol%, the conversions of ethylbenzene stayed near to the result of using 10 mol% (entries 7–9). These means that the catalytic ability was not improved obviously by increasing the amounts of the catalysts further above and beyond 10 mol%.

Table 2. The oxidation of ethylbenzene with different amounts of DMG and NHPI.[a]

Entry	DMG/NHPI [mol%/mol%]	Conversion [%]	Selectivity [%]		
			AcPO	PEA	PEHP
1	10/10	74.5	74.9	17.4	7.7
2	5/5	51.6	71.3	12.5	16.2
3	5/10	54.3	69.5	15.3	15.2
4	10/5	61.2	68.9	14.2	16.9
5	5/15	56.9	70.1	16.2	13.7
6	15/5	55.3	70.4	17.7	11.9
7	10/15	71.2	72.2	13.3	14.5
8	15/10	75.4	67.8	18.2	14.0
9	15/15	75.5	61.5	19.5	19.0

[a] *Reaction conditions:* 16 mmol ethylbenzene, 10 mL CH_3CN, 0.3MPa O_2, 80 °C, 6 h.

The effect of temperature on the oxidation of ethylbenzene was investigated and is summarized in Table 3. As expected, with the reaction temperature rising, the conversion of ethylbenzene increased with the concomitant gradual increase of AcPO and the decrease of PHEP in the selectivities. When the temperature was 80 °C, 74.5% conversion and 74.9% selectivity of AcPO were obtained in the presence of

Table 3. The effect of reaction temperature on oxidation of ethylbenzene.[a]

Entry	Temperature [°C]	Conversion [%]	Selectivity [%]		
			AcPO	PEA	PEHP
1	40	36.2	59.7	18.9	21.4
2	60	56.6	68.9	19.1	12.0
3	70	68.3	70.5	18.8	10.7
4	80	74.5	74.9	17.4	7.7
5	90	74.8	76.7	15.8	7.5
6	100	75.7	76.8	16.0	7.2

[a] *Reaction conditions:* 16 mmol ethylbenzene, 10 mol% DMG, 10 mol% NHPI, 10 mL CH_3CN, 0.3 MPa O_2, 6 h.

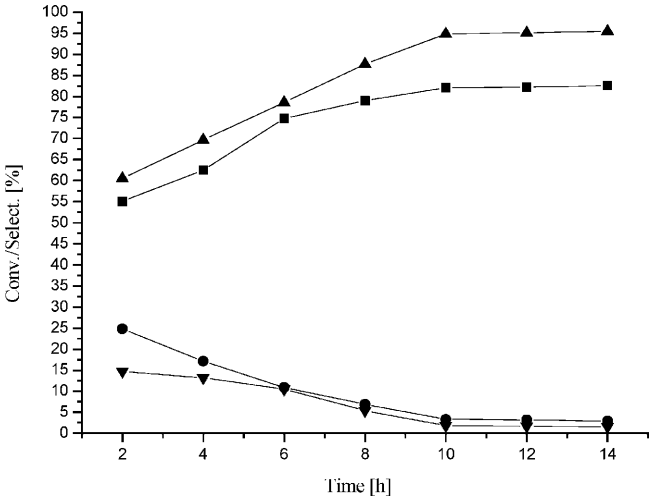


Figure 1. Time course of the oxidation of ethylbenzene by the DMG/NHPI system: (■) ethylbenzene; (▲) AcPO; (▼) PEA; (●) PEHP. *Reaction conditions:* 16 mmol ethylbenzene, 10 mol% DMG, 10 mol% NHPI, 10 mL CH_3CN, 80 °C, 0.3 MPa O_2.

10 mol% NHPI and 10 mol% DMG during a 6 h reaction period. However, the oxidations changed only very slightly even at higher temperatures (entries 4–6).

The influence of reaction time on the catalytic oxidation of ethylbenzene by DMG/NHPI is shown in Figure 1. As illustrated, the conversion of ethylbenzene increased with prolonging the reaction time. Simultaneously, the selectivity of AcPO continuously increased, and the selectivities of PEA and PEHP decreased due to the continuous decomposition of PEHP to PEA, which was further oxidized to yield more AcPO. However, after 10 h the conversion was changed slowly and became stagnated near 80%. As a result, in a 10 h reaction course, 82.1% ethylbenzene was oxidized with 94.9% selectivity of AcPO.

Table 4 shows the oxidation results under the different pressures of molecular oxygen. Below 0.3 MPa a positive influence of pressure on the reaction rate was observed clearly, the pressure increase leading to an increase in conversion (entries 1–3). Above 0.3 MPa the pressure influence is no longer obvious with no more than 78% conversion (entries 4 and 5). However, the oxidation still reached a higher conversion on prolonging the reaction time under 0.3 MPa (Figure 1). So 0.3–0.5 MPa of molecular oxygen seems to be enough for the oxidation.

Oxidation of Different Hydrocarbons Catalyzed by DMG/NHPI

In order to further probe the potential, this non-metal catalytic system was employed to catalyze the oxygenation of various substrates under mild conditions

Table 4. The oxidation of ethylbenzene under different dioxygen pressures.[a]

Entry	Pressure [MPa]	Conversion [%]	Selectivity [%]		
			AcPO	PEA	PEHP
1	0.1	47.7	71.2	19.4	9.4
2	0.2	68.3	72.7	18.3	9.0
3	0.3	74.5	74.9	17.4	7.7
4	0.5	76.5	76.1	15.0	8.9
5	0.7	77.9	75.7	15.2	9.1

[a] *Reaction conditions:* 16 mmol ethylbenzene, 10 mol% DMG, 10 mol% NHPI, 10 mL CH_3CN, 80 °C, 6 h.

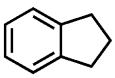
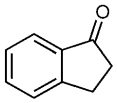
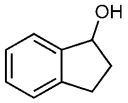
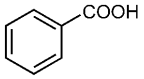
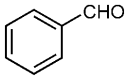
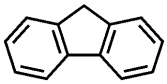
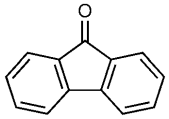
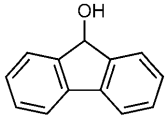
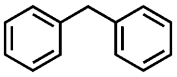
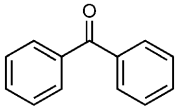
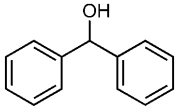
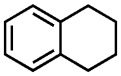
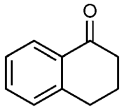
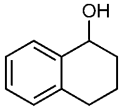
(Table 5). 88.1% of indane was oxidized to afford indanone with 75.3% selectivity at 80 °C under 0.5 MPa O_2 for 8 h (entry 1). Toluene and fluorene (entry 2, 3) were also converted into the benzoic acid and fluorenone with satisfactory conversions (57.8% and 67.3%), respectively. Diphenylmethane was converted in 66.1% conversion with 90.6% selectivity of benzophenone at 80 °C for 6 h (entry 4). Tetralin could also be oxidized with the corresponding ketone as the main product.

Suggested Catalytic Mechanism of Oxidation

As the data above show, for the aerobic oxidation of ethylbenzene, DMG had no catalytic effect, NHPI had only a slight effect, and the combination of NHPI and DMG had a high catalytic ability. In order to further understand this finding, several experiments were carried out. Firstly, hydroquinone (5 mol%), a free radical scavenger, was added into the oxidation of ethylbenzene catalyzed by DMG/NHPI. The result that no oxidation occurred indicated that the oxidation followed a radical pathway. Secondly, dimethylglyoxime ester was used to replace DMG in the above catalytic oxidation of ethylbenzene. When the oxidation of ethylbenzene was carried out at 80 °C for 6 h under the pressure of 0.3 MPa, it only gave the conversion of 23.5%, which was consistent with the result of using NHPI alone under the same conditions. This implied that dimethylglyoxime ester had no catalytic effect, and that the *N*-hydroxy groups of DMG played a key role in the catalytic oxidation.

Accordingly, the NHPI-catalyzed aerobic oxidations follow a free radical route, and are initiated and propagated by a nitroxyl radical, phthalimide *N*-oxyl radical (PINO), which comes from the hydrogen abstraction of *N*-hydroxy of NHPI by the used mediators or their oxidized species.[3] Ishii reported that ethylbenzene could be efficiently oxidized by molecular oxygen in the presence of NHPI and Co(OAc)$_2$.[3b,12] Generally, the bond dissociation energies of the O–H unit of oximes are lower than that of the

Table 5. Oxidation of various hydrocarbons by the NHPI/DMG system.[a]

Entry	Hydrocarbon	Time [h]	Conversion [%]	Main Products and Selectivity [%]			
1		8	88.1		75.3		10.4
2		8	57.8		83.1		10.7
3		10	67.3		88.7		11.3
4		6	66.1		90.6		9.4
5		6	84.2		82.2		9.7

[a] *Reaction conditions:* 2 mL liquid substrate or 2 mmol solid substrate, 10 mol% NHPI, 10 mol% DMG, 10 mL CH_3CN, 80 °C, 0.5 MPa O_2.Coversion and selectivity were determined by GC.

O–H of NHPI,[13] meaning that oximes undergo abstraction of hydrogen more easily to form the corresponding *N*-oxyl radical. However, at 80 °C under 0.3 MPa O_2 for 6 h, the combination of DMG and $Co(OAc)_2$ gave only 9.8% conversion of ethylbenzene, which was quite near to the result (10.3%) of using $Co(OAc)_2$ alone under the same conditions. These facts indicated that the corresponding *N*-oxyl radical of DMG could not work like PINO to promote the radical aerobic oxidation, even though it was formed in the reaction.

So a possible catalytic mechanism of oxime/NHPI in the aerobic oxidation was proposed and is displayed in Scheme 1. The first step of the reaction was thought to involve the corresponding *N*-oxyl radical of oximes, which was formed by the reaction of oxime and dioxygen. And then this *N*-oxyl radical abstracted hydrogen from NHPI to recover to oxime. Simultaneously, NHPI was converted to PINO, which abstracted a hydrogen atom from the substrates to form alkyl radicals, thus propagating the autoxidation chain.

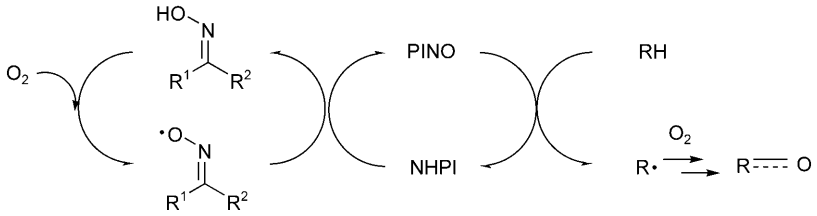
Conclusions

Summarising, we have developed a novel catalytic system consisting of DMG and NHPI for the aerobic oxidation of hydrocarbons. The synergistic effect of DMG and NHPI ensures its efficient catalytic ability. By its catalysis, hydrocarbons can be oxidized to the corresponding oxygenated compounds with high conversions and high selectivities under mild conditions. This metal-free catalytic oxidation method has an environmentally friendly feature and provides an attractive method which has long been desired in the chemical industry.

Experimental Section

All starting materials and catalysts were purchased from commercial sources and used without further treatment.

All the catalytic reactions were performed in an 80-mL stainless steel autoclave equipped with a magnetic stirrer.



Scheme 1. A possible reaction mechanism for the catalytic cycle of the DMG/NHPI system.

Typically, 2 mL (16 mmol) ethylbenzene, 10 mL acetonitrile, the desired amount of DMG and NHPI were added into the autoclave. The reactor was flushed three times with O_2 and pressurized to 0.3 MPa, and then heated to the desired temperature with stirring. During the reaction the O_2 pressure was kept constant by supplying dioxygen.

The oxidation products were identified by GC-MS and quantified by GC. The conversion of ethylbenzene, and the selectivities of acetophenone (AcPO) and 1-phenylethanol (PEA) were determined by calibration curves. The yield of 1-phenylethyl hydroperoxide (PEHP) could not be directly measured by GC due to its decomposition to AcPO in GC analysis.[10] In addition, PEHP can be converted quantitatively to PEA by excess Ph_3P at room temperature.[6,10] Thus the amount of PEHP can be accurately quantified by treatment of the mixture with excess Ph_3P for 1 h and a second GC measurement. For all the other substrates, the conversions and selectivities were calculated by GC calibration curves.

Acknowledgements

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References

[1] a) P. R. Schreiner, A. A. Fokin, *Chem. Rec.* **2004**, *3*, 247–257; b) E. N. Jacobson, *Adv. Synth. Catal.* **2004**, *346*, 109; c) M. Beller, *Adv. Synth. Catal.* **2004**, *346*, 107–108;.

[2] a) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329–2363; b) A. K. Suresh, M. M. Sharma, T. Sridhar, *Ind. Eng. Chem. Res.* **2000**, *39*, 3958–3997; c) C. I. Herrerias, X. Q. Yao, Z. P. Li, C. J. Li, *Chem. Rev.* **2007**, *107*, 2546–2562; d) A. A. Fokin, P. R. Schreiner, *Adv. Synth. Catal.* **2003**, *345*, 1035–1052; e) J. M. Thomas, R. Raja, *Chem. Commun.* **2001**, *8*, 675–687.

[3] a) F. Recupero, C. Punta, *Chem. Rev.* **2007**, *107*, 3800–3842; b) Y. Ishii, S. Sakaguchi, T. Iwahama, *Adv. Synth. Catal.* **2001**, *343*, 393–427; c) R. A. Sheldon, I. W. C. E. Arends, *Adv. Synth. Catal.* **2004**, *346*, 1051–1071; d) C. Galli, P. Gentili, O. Lanzalunga, *Angew. Chem.* **2008**, *120*, 4868–4874; *Angew. Chem. Int. Ed.* **2008**, *47*, 4790–4796; e) Y. Aoki, S. Sakaguchi, Y. Ishii, *Tetrahedron* **2006**, *62*, 2497–2500; f) G. Y. Yang, L. W. Zheng, G. H. Wu, X. S. Lin, M. P Song, *Adv. Synth. Catal.* **2007**, *349*, 2445–2448; g) R. A. Sheldon, I. W. C. E. Arends, *J. Mol. Catal. A: Chem.* **2006**, *251*, 200–214.

[4] Y. Aoki, S. Sakaguchi, Y. Ishii, *Adv. Synth. Catal.* **2004**, *346*, 199–202.

[5] S. Tsujimoto, S. Sakaguchi, Y. Ishii, *Tetrahedron Lett.* **2003**, *44*, 5601.

[6] a) G. Y. Yang, Y. F. Ma, J. Xu, *J. Am. Chem. Soc.* **2004**, *126*,10542; b) G. Y. Yang, Q. H. Zhang, H. Miao, X. L. Tong, J. Xu, *Org. Lett.* **2005**, *7*, 263–266; c) Q. H. Zhang, C. Chen, H. Ma, H. Miao, W. Zhang, Z. Q. Sun, J. Xu, *J. Chem. Technol. Biotechnol.* **2008**, *83*, 1364–1369.

[7] Z. T. Du, Z. Q. Sun, W. Zhang, H. Miao, H. Ma, J. Xu, *Tetrahedron Lett.* **2009**, *50*, 1677–1680.

[8] X. L. Tong, J. Xu, H. Miao, J. Gao, *Tetrahedron Lett.* **2006**, *47*, 1763–1766.

[9] K. Matsunaka, T. Iwahama, S. Sakaguchi, Y. Ishii, *Tetrahedron Lett.* **1999**, *40*, 2165–2168.

[10] S. Evans, J. R. L. Smith, *J. Chem. Soc. Perkin Trans. 2* **2001**, 174–180.

[11] H. Ma, J. Xu, Q. H. Zhang, H. Miao, W. H. Wu, *Catal. Commun.* **2007**, *8*, 27–30.

[12] T. Iwahama, G. Hatta, S. Sakaguchi, Y. Ishii, *Chem. Commun.* **2000**, 163–164.

[13] 13] N. Koshino, Y. Cai, J. H. Espenson, *J. Phys. Chem. A:* **2003**, *107*, 4262–4267.

