DOI: 10.1002/adsc.200505183

Highly Efficient and Metal-Free Aerobic Hydrocarbons Oxidation Process by an *o*-Phenanthroline-Mediated Organocatalytic System

Xinli Tong, Jie Xu,* Hong Miao

State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Graduate School of the Chinese Academy of Sciences, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian, Liaoning 116023, People's Republic of China,
Fax: (+86)-(0)411-8437-9245, e-mail: xujie@dicp.ac.cn

Received: May 1, 2005; Accepted: August 30, 2005

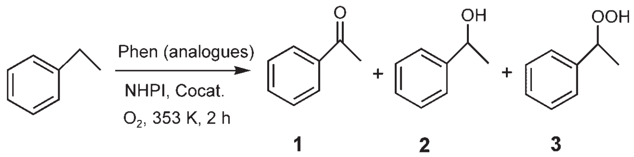
Supporting Information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: A highly efficient *o*-phenanthroline-mediated, metal-free catalytic system has been developed for oxidation of hydrocarbons with dioxygen in the presence of *N*-hydroxyphthalimide; various hydrocarbons were efficiently and high selectively oxidized, e.g., ethylbenzene to acetophenone in 97% selectivity and 76% conversion, under mild conditions.

Keywords: C–H activation; hydrocarbons; molecular oxygen; organic catalysis; oxidation; *o*-phenanthroline

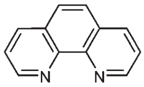
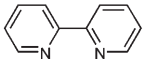
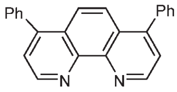
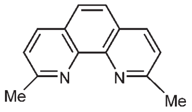
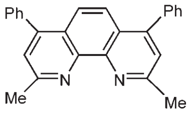
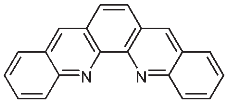
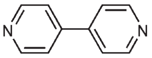
The aerobic selective oxidation of hydrocarbons is a major goal of today's research in catalysis as selectively oxidized hydrocarbons can be used as feedstock for the preparation of fine chemicals.[1] In catalysis research field, catalytic efficiency and product selectivity remain a challenge when molecular oxygen is employed as terminal oxidant.[2] Traditional approaches for oxidation are based on metal-catalyzed activation of hydrocarbons.[3] Aiming at improving oxidation efficiency, Ishii's group and others developed an efficient catalytic system of *N*-hydroxyphthalimide (NHPI) combined with metal mediators (cobalt, manganese, etc.), which exhibited considerable activity in oxidation processes.[4] Recently, due to concerns of metal toxicity and metal-sensitive products, extensive research has been carried out on metal-free C–H activations,[5] thus combining organic mediators with NHPI becomes an ideal catalytic system. Our group has reported a biomimetic non-metal system composed of anthraquinones, HY zeolite and NHPI.[6] Excellent selectivity for hydrocarbon oxidation was obtained. In the above autoxidation processes, the active catalytic species of phthalimide *N*-oxyl radical (PINO) originated from NHPI *via* proton and electron transfer with the assistance of catalyst mediators. *O*-Phenanthroline (Phen) or bipyridine (or analogues) in combination with a metal has been employed to the electron-transfer process or to some oxidation processes,[7] but has rarely employed for hydrocarbon oxidation in the absence of metal complexes. Herein, focusing on more efficient organic mediators, we have developed a new *o*-phenanthroline (or analogues)-mediated, metal-free catalytic system for the oxidation of hydrocarbons in the presence of NHPI and a cocatalyst. In this communication, molecular bromine (Br_2), which has shown a particular promotion effect in some oxidation process,[8] was chosen as a cocatalyst.

To test the efficiency of our catalytic system, ethylbenzene was used as a model substrate (Scheme 1). The reaction was carried out under 0.3 MPa of O_2 at 353 K for 2 h. Table 1 shows the results of oxidation using Phen or different analogues as catalyst mediators in the presence of NHPI and Br_2. When Phen was employed, a 76% conversion and 97% selectivity for acetophenone (**1**) was obtained (entry 1). The conversion decreased (67 or 65%) and the selectivity for **1** was almost unchanged when 2, 2′-bipyridine or bathophenanthroline replaced Phen as catalyst mediators (entries 2 and 3). However, when neocuproine, bathocuproin, or 2,2′-bichinolin was employed, the conversion (35% –49%) and selectivity (75% –88%) for **1** were evidently reduced (entries 4–6). Even as expected, only 28% conversion and 67% selectivity for **1** were obtained when 4, 4′-bipyridine was used instead of Phen (entry 7). It can be seen that Phen is a most efficient catalyst mediator, and differences in the oxidations mediated by different analogues are probably ascribed to effects of conjugated structures or substituents.



Scheme 1. Oxidation of ethylbenzene with molecular oxygen.

Table 1. Oxidation of ethylbenzene by Phen (or analogues)-mediated catalysis.[a]

Entry	Mediator	Conversion[b] [%]	Product selectivity [%]		
			1	**2**	**3**
1		76	97	3	< 1
2		67	96	3	1
3		65	97	2	1
4		35	75	20	5
5		45	87	11	2
6		49	88	11	1
7		28	67	17	17

[a] Reaction conditions: the reaction of ethylbenzene was performed on a 1-mL scale, in the presence of NHPI (7.5 mol %), Phen hydrate or analogues (2.5 mol %), Br_2 (3.0 mol %), in 10 mL CH_3CN, pressure = 0.3 MPa, time = 2 h, temperature = 353 K.

[b] The data were obtained by GC and GC-MS analysis using 1, 3-dichlorobenzene as an internal standard.

As indicated in Table 2, various hydrocarbons have been successfully oxidized using Phen as a catalyst mediator. Tetralin was oxidized to 1-tetralone in 98% selectivity at 93% conversion only for 1 h (entry 1). When indan was oxidized, an 88% conversion and 89% selectivity for 1-indanone was obtained (entry 2). Moreover, no induction periods were observed during their oxidation, possibly due to the C–H bonds being affected by ring strain. In the case of diphenylmethane, 100% selectivity for benzophenone, as no by-products were detected by GC, was obtained at 34% conversion (entry 3). In addition, oxidations of cyclohexane and toluene were also performed to extend the present method with our catalytic system. It was found that 14% or 25% of toluene was oxidized after 3 h or 5 h (entries 4 and 5), while 21% or 48% conversion was obtained in the oxidation of cyclohexane after 2 h or 5 h (entries 6 and 7). The major oxygenated products were ketone/aldehyde and acid/esters. In the mean time, GC-MS measurements indicated that a few brominated products existed in the reaction, which was probably affected by the randomness of radical reactions. For the oxidation of cyclohexane, the selectivity of cyclohexanone (25 to 22%) changed a little when the reaction time was prolonged and the conversion was enhanced. However, for the oxidation of toluene, the selectivity for benzaldehyde (47 to 20%) was obviously reduced along with the increase of the conversion, which suggests that the aldehyde was not stable in this radical reaction. From these results, it could be seen that the remarkable conversion and selectivity of oxygenated hydrocarbons have been demonstrated under mild conditions when our metal-free organocatalytic system was employed.

In order to clearly reveal the function and character of catalyst components, compared data are summarized in Table 3. It was observed that only 3% of ethylbenzene was oxidized when 7.5 mol % NHPI was used individually (entry 1), and oxidation hardly occurred when 2.5 mol % Phen was solely employed (entry 2). But then, when Phen and NHPI were coupled as a catalytic system, the conversion was improved to 9% but 71% selectivity for 1-phenylethyl hydroperoxide (**3**) was obtained (entry 3). In succession, we investigated the oxidation of ethylbenzene by Br_2, NHPI-Br_2 or Phen-Br_2 under the same reaction conditions; nevertheless, only 1%, 3% or 2% of ethylbenzene was respectively oxidized (entries 4–6). Furthermore, when bromine ion was used as a cocatalyst in the presence of Phen and NHPI, a promising result (43% conversion and 75% selectivity for **1**) was obtained (entry 7). Owing to PINO

Table 2. Oxidation of various substrates by the Phen-mediated catalytic system.[a]

Entry	Substrate	t [h]	Conversion[b] [%]	Products selectivity [%]			
1	Tetralin	1	93	1-Tetralone	98	1-Tetralol	2
2	Indan	1	88	1-Indanone	89	1-Indanol	11
3[c]	Diphenylmethane	2	34	Benzophenone	100	–	–
4	Toluene	3	14 [d]	Benzaldehyde	47	Benzoic acid	50
5	Toluene	5	25[d]	Benzaldehyde	20	Benzoic acid	78
6[c]	Cyclohexane	2	21[e]	Cyclohexanone	25	AE[f]	71
7[c]	Cyclohexane	5	48[e]	Cyclohexanone	22	AE[f]	75

[a] General reactions condition: reactants were performed on a 1 mL scale, in the presence of NHPI (7.5 mol %), Phen hydrate (2.5 mol %), Br_2 (3.0 mol %), in 10 mL CH_3CN, pressure = 0.3 MPa, temperature = 353 K.

[b] The data were obtained by GC and GC-MS analysis using 1,3-dichlorobenzene as an internal standard.

[c] Reaction was performed at 373 K in 5 mL CH_3CN and 5 mL CCl_4.

[d] 1,2,4,5-Tetramethylbenzene as an internal standard.

[e] Toluene as an internal standard.

[f] AE represents adipic acid or ester.

Table 3. Oxidation of ethylbenzene in different catalyst combinations.[a]

Entry	Catalyst	Conversion [%]	Products selectivity [%]		
			1	**2**	**3**
1	NHPI	3	9	12	79
2	Phen	0	–	–	–
3	Phen + NHPI	9	11	18	71
4	Br_2	1	28	47	25
5	NHPI + Br_2	3	18	80	2
6	Phen + Br_2	2	86	13	1
7[b]	Phen + NHPI + NaBr	43	75	12	13
8[c]	Phen + Br_2	4	72	25	3
9[d]	Phen + Br_2 + NaBr	6	71	14	15

[a] Reaction conditions and analytical methods were similar with the situations in Table 1.

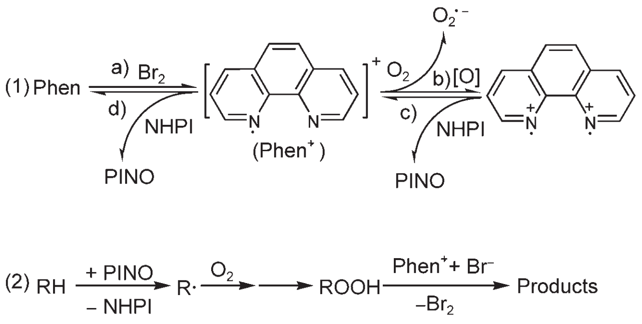
[b] 5.0 mol % NaBr was employed.

[c] 12.5 mol % Phen and 15.0 mol % Br_2 were employed.

[d] 5.0 mol % Phen, 3.0 mol % Br_2 and 5.0 mol % NaBr were employed.

and bromine radical being provided with similar thermodynamic and kinetic properties in C–H abstraction reactions,[4] the control experiments were carried out with larger contents of Phen-Br_2 and the combination of Phen-Br_2-Br^- (entries 8 and entry 9), and only 4% and 6% conversion were obtained, which showed that the bromine radical could rarely exist and PINO radical could mainly perform activation of C–H bond in this organocatalytic oxidation. All these results directly exhibited the importance of Phen-mediation and the necessity for cooperating functions of the catalyst components in the oxidation process.

Sequentially, several parameters have been investigated about the reaction mechanism. No oxidation occurred in the presence of hydroquinone, which confirmed the free radical pathway of the reaction. In addition, after Phen, NHPI and Br_2 were mixed without any substrate in acetonitrile, the solution's color gradually changed from brown-red (color of Br_2) to yellow (color of PINO),[9] which proved visually the production of PINO radicals. Moreover, PINO signals could be found by means of *in situ* FT-IR spectroscopy. Now that the reaction can proceed efficiently, a catalytic oxidation cycle must exist. A proposed mechanism is shown in Scheme 2. From our viewpoint, *p*-phenylenediamines containing tertiary nitrogens are facilely oxidized to the cation radicals by Br_2 or electrode through a single electron transfer process,[10] so Phen can potentially be converted to cation radicals through single-electron oxidation of the nitrogen atom in the beginning of the reaction, then the cation radicals promote the generation of PINO radical under the metal-free conditions *via* electron and proton transfer between cation radicals and NHPI (E1 of Scheme 2). The next step involves the hydrogen atom abstraction from the hydrocarbon by PINO, and the resulting hydrocarbon radical being trapped by dioxygen provides the peroxy radicals which are eventually converted into products through hydroperoxide (E2). Otherwise, the one electron-deficient Phen cation radical can be probably produced and acti-



Scheme 2. Proposed mechanisms for hydrocarbon oxidation using the Phen-mediated catalytic system.

vates molecular oxygen. Further investigations about the reaction mechanism, especially including more direct information about the PINO radical and Phen cation radicals in the oxidation, are underway.

In summary, a new Phen (or analogues)-mediated, metal-free organocatalytic system has been developed which can efficiently and with high selectivity promote aerobic oxidation of various hydrocarbons under mild conditions, and will therefore constitute a promising strategy in the petrochemical industry.

Experimental Section

Reagents

Ethylbenzene and other substrates were purified by distillation. Spectro-grade acetonitrile was purchased from Tedia Company, Inc. All other reagents were of analytical grade. Oxygen supplied in a high-pressure cylinder was used through a reducing valve without further treatment.

General Procedure for Oxidation of Various Hydrocarbons

All oxidation experiments were performed in a 100-mL autoclave equipped with magnetic stirring and automatic temperature control. A typical procedure for the oxidation of ethylbenzene was as follows: an acetonitrile (10 mL) solution of ethylbenzene (1 mL, 8.3 mmol), NHPI (7.5 mol %), Phen (2.5 mol %), and bromine (3.0 mol %) was charged into the reactor; The atmosphere inside were replaced with oxygen before the reactor was sealed. Under stirring, the autoclave was preheated to 353 K, and then oxygen was charged to 0.3 MPa and kept for 2 h. After the reaction, the autoclave was cooled, and the excess gas was purged.

Products Analysis

The products were analyzed with the internal standard technique by gas chromatography using a flame ionization detector (all products were determined on GC-MC). Besides, in order to quantify the selectivity of the oxidation products of various organic substrates, the reaction mixtures were all treated with an excess of Ph_3P for 1 h after the first GC measurement and were analyzed again. For example, in the oxidation of ethylbenzene (Scheme 1), due to the fact that the compound **3** could be reduced quantitatively to **2** by Ph_3P at room temperature, the selectivity of **1**, **2** and **3** could be accurately attained after a second GC measurement.

Typical Separation Procedure for Acetophenone (1)

After ethylbenzene was oxidized, the reaction mixture was transferred into a flask and an aqueous solution of semicarbazide hydrochloride and sodium acetate was added. The obtained liquid mixtures were stirred for 4 h under reduced pressure and left in a refrigerator for 5 h, and then the resulting solid was collected by filtration. The solid mixtures, which were composed of catalysts and formed semicarbazone of **1**, were washed with diethyl ether to remove ethylbenzene and byproducts. In the following, the washed solid was transferred into a two-neck flask and dissolved in oxalic acid and water, and then was refluxed for 2 h. The regenerated **1** was distilled out by steam distillation. The distillate was saturated with sodium chloride and extracted with diethyl ether. After being dried, the diethyl ether layer was distilled to obtain pure **1** as a liquid. The purity was more than 99% from GC analysis. The yield was 71% (Entry 1 in Table 1).

Supporting Information

Detailed GC measurement conditions and correlative IR spectra are contained in the Supporting Information.

Acknowledgements

This work was financially supported by the National Natural Science Foundation of China (Project 20473088) and the National High Technology Research and Development Program of China (Project 2004AA32G020).

References and Notes

[1] a) R. A. Sheldon, J. K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds,* Academic Press, New York, **1981**; b) G. A. Olah, A. Molnár, *Hydrocarbon Chemistry*, 2nd edn., John Wiley & Sons: Hoboken, NJ, **2003**; c) W. D. Jones, *Science* **2000**, 287, 1942–1943.

[2] a) D. H. R. Barton, A. E. Martell, D. T. Sawyer, *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*, Plenum Press, New York, **1993**; b) R. A. Sheldon, J. Dakka, *Catal. Today* **1994**, *19*, 215–245; c) A. K. Suresh, *Ind. Eng. Chem. Res.* **2000**, *39*, 3958–3997; d) R. A. Periana, G. Bhalla, W. J. Tenn, K. J. H. Young, X. Liu, O. Mironov, CJ Jones, V. R. Ziatdinov, *J. Mol. Catal.* **2004**, *220*, 7–25; e) M. Beller, *Adv. Synth. Catal.* **2004**, *346*, 107–108.

[3] a) A. E. Shilov, G. B. Shul'pin, *Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of*

Metal Complexes, Kluwer Academic Publishers, Dordrecht, **2000**; b) G. B. Shul'pin, *C. R. Chimie* **2003**, *6*, 163–178.

[4] a) Y. Ishii, S. Sakaguchi, T. Iwahama, *Adv. Synth. Catal.* **2001**, *343*, 393–427; b) A. Shibamoto, S. Sakaguchi, Y. Ishii, *Tetrahedron Lett.* **2002**, *43*, 8859–8861; c) R. Arnaud, A. Milet, C. Adamo, C. Einhorn, J. Einhorn, *J. Chem. Soc. Perkin Trans. 2* **2002**, 1967–1972; d) R. A. Sheldon, I. W. C. E. Arends, *Adv. Synth. Catal.* **2004**, *346*, 1051–1071; e) L. S. Vondervoort, S. Bouttemy, F. Heu, K. Weissenböck, P. L. Alsters *Eur. J. Org. Chem.* **2003**, *68*, 578–580; f) F. Minisci, F. Recupero, A. Cecchetto, C. Gambarotti, C. Punta, R. Paganelli, *Org. Proc. Res. & Dev.* **2004**, *8*, 163–168.

[5] a) W. Adam, C. R. Saha-Möller, P. A. Ganeshpure, *Chem. Rev.* **2001**, *101*, 3499–3548; b) H. Bjørsvik, L. Liguori, J. A. V. Merinero, *J. Org. Chem.* **2002**, *67*, 7493–7500; c) K. Ohkubo, S. Fukuzami, *Org. Lett.* **2000**, *2*, 3647–3650; d) A. A. Fokin, P. R. Schreiner, *Adv. Synth. Catal.* **2003**, *345*, 1035–1052; e) A. Córdova, H. Sundén, M. Engqvist, I. Ibrahem, J. Casas, *J. Am. Chem. Soc.* **2004**, *126*, 8914–8915.

[6] a) G. Yang, Y. Ma, J. Xu, *J. Am. Chem. Soc.* **2004**, *126*, 10542–10543; b) G. Yang, Q. Zhang, H. Miao, X. Tong, J. Xu, *Org. Lett.* **2005**, *7*, 263–266.

[7] a) G.-J. ten Brink, I. W. C. E. Arends, R. A. Sheldon, *Science* **2000**, ^{287}, 1636–1639; b) M. M. Richter, *Chem. Rev.* **2004**, ^{104}, 3003–3036; c) P. Gamez, I. W. C. E. Arends, J. Reedijk, R. A. Sheldon, *Chem. Commun.* **2003**, 2414–2415; d) C. K. Barlow, S. Wee, W. D. McFadyen, R. A. J. O'Hair, *Dalton Trans.* **2004**, 3199–3204.

[8] R. Liu, X. Liang, C. Dong, X. Hu, *J. Am. Chem. Soc.* **2004**, *126*, 4112–4113.

[9] M. Masui, T. Ueshima, S. Ozaki, *Chem. Commun.* **1983**, 479–480.

[10] a) L. Michaelis, M. P. Schubert, S. Granick, *J. Am .Chem. Soc.* **1939**, **61**, 1981–1992; b) R. Forster, *Organic Charge-Transfer Complexes*; Academic Press: New York, **1969**; c) B. A. Kowert, L. Marcoux, A. J. Bard, *J. Am. Chem. Soc.* **1972**, *94*, 5538–5550; d) K. Hu, D. H. Evans, *J. Electronanl. Chem.* **1997**, *423*, 29–35; e) A. M. M. Rawashdeh, C. Sotiriou-Leventis, X. Gao, N. Leventis, *Chem. Commun.* **2001**, 1742–1743.