Organic Process Research & Development **2005**, *9,* 297–301

Highly Efficient, Mild, Bromide-Free and Acetic Acid-Free Dioxygen Oxidation of *p*-Nitrotoluene to *p*-Nitrobenzoic Acid with Metal Phthalocyanine Catalysts

Xufeng Song,[‡] Yuanbin She,*,[†,‡] Hongbing Ji,[§] and Yanhui Zhang[⊥]

School of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, P.R. China, Institute of Green Chemistry, Beijing University of Technology, Beijing 100022, P.R. China, School of Chemical and Energy Engineering, South China University of Technology, Guangzhou 510640, P.R. China, and College of Life Science and Bio-engineering, Beijing University of Technology, Beijing 100022, P. R. China

Abstract:

Four metal tetracarboxyl phthalocyanines were synthesized and characterized by elemental analysis and mass spectrometry. *p*-Nitrobenzoic acid was efficiently prepared in high yield from bromide-free and acetic acid-free aerobic oxidation of *p*-nitrotoluene using metal phthalocyanines as catalysts under mild conditions in alkali−methanol solution. Up to 88.8% isolated yield of *p*-nitrobenzoic acid was obtained with the catalysis of tetracarboxyl phthalocyanine cobalt (0.13 mol %, based on the moles of *p*-nitrotoluene) optionally combined with a small amount of dimethylformamide in the presence of 2.0 MPa dioxygen at 30−60 °C. The effect on catalytic performance of a carboxyl group introduced into the phthalocyanine ring was further discussed on the basis of metal coordination chemistry theory.

Introduction

p-Nitrobenzoic acid is of great importance as an essential intermediate of pharmaceutical, organic synthesis, perfumery, pigment, antioxidant for grease lubrication, metal antirust agents, and the like. Conventionally, for oxidation of alkyl benzenes, stoichiometric oxidants such as nitric acid, potassium permanganate, potassium dichromate, sodium hypochlorite, or organic peroxides are necessary for effective conversion. However, these hazardous and/or toxic oxidants generate copious amounts of wastes. Therefore, using a green oxidant such as molecular oxygen[1,2] or ozone[3−5] is gathering much attention according to the principle of green chemistry. It is well-known that molecular oxygen could hardly be activated in mild conditions. As a result, catalysts such as cobalt bromide and manganese salt, as well as solvents such as acetic acid are unavoidable, especially when strong electron-withdrawing substituents such as the nitro group are introduced into alkyl benzenes, even under high reaction temperature and high pressure of air/dioxygen. However, the bromide ion or acetic acid may bring undesirable side reactions and causticity on the devices via bromination or decarboxylation.[6] Alternatively, although replacement of conventional oxidants with H_2O_2 has shown unexampled advantages in certain aspects compared with molecular oxygen, such as reaction activity, three industrial wastes, and environmental protection, H_2O_2 will self-degrade acutely and invert into inert O_2, which has to be reactivated, in the presence of transitional metal ions or complexes thereof at relatively high cost. Sawatari and coauthors[1] developed an efficient bromide-free catalytic system for the oxidation of nitrotoluenes. Yet, an expensive carbon radical-producing catalyst such as *N*-hydroxylphthalimide (NHPI), cobalt salt, manganese salt, and acetic acid was used, and a relatively high temperature such as 130 °C was adopted.

In our endeavor to research toward oxidation using biomimetic catalysts such as metal phthalocyanines and metal porphyrins,[7−10] many oxidations could be achieved under mild conditions compared with the conventional ones. Although Chandalia and Mukhopadhyay[2] reported the moderate yield of *p*-nitrobenzoic acid catalyzed by cobalt phthalocyanine, the yield was not satisfactory. In the present contribution, the above reaction with different catalysts was systematically investigated in detail, and the significant enhancement of catalytic activity has been achieved by introducing a carboxyl group into the phthalocyanine rings and by adding a cosolvent.

Results and Discussions

In our investigation, aerobic oxidation of *p*-nitrotoluene to the corresponding *p*-nitrobenzoic acid was catalyzed by different metal phthalocyanine catalysts. Methanol, as an alternative solvent, instead of conventional solvents such as

---

* Corresponding author: Prof. Yuanbin She. E-mail: sheyb@bjut.edu.cn. Telephone and fax: +86-10-67392695.

[†] School of Chemistry and Chemical Engineering, Hunan University.

[‡] Institute of Green Chemistry, Beijing University of Technology.

[§] School of Chemical and Energy Engineering, South China University of Technology.

[⊥] College of Life Science and Bio-engineering, Beijing University of Technology.

(1) Sawatari, N.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett*. **2003**, *44*, 2053−2056.

(2) Chandalia, S. B.; Mukhopadhyay, S. *Org. Process Res. Dev*. **1999**, *3*, 109−113.

(3) Galstyan, A. G.; Tyupalo, N. F.; Andreev, P. Y. *Kinet. Catal*. **2003**, *44*, 82−85.

(4) Galstyan, A. G.; Tyupalo, N. F. *Pet. Chem*. **2002**, *42*, 314−317.

(5) Galstyan, A. G.; Tyupalo, N. F.; Patapenko, E. V.; Andreev, P. Y. *Russ. J. Appl. Chem*. **2001**, *74*, 1777−1779.

(6) Zhang, S.; Xin, Z. *Preparation Handbook of Fine Organic Chemical Engineering (Chinese)*; Beijing: Science and Technology Reference Press, 2000; pp 349−352.

(7) Yuan, Y.; Ji, H. B.; Chen, Y. X.; Han, Y.; Song, X. F.; She, Y. B.; Zhong, R. G. *Org. Process Res. Dev*. **2004**, *8*, 418−420.

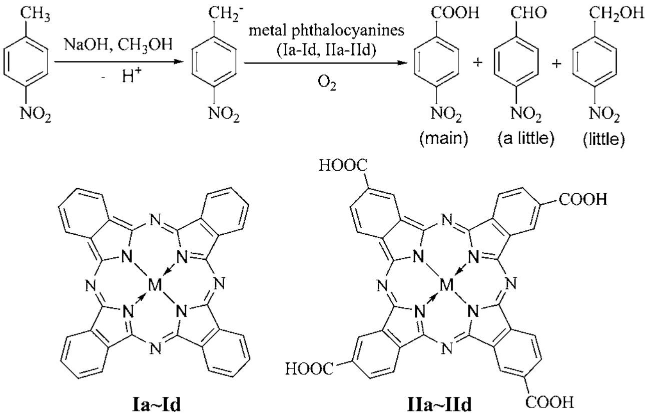
(8) She, Y. B.; Fan, L. L.; Zhang, Y. H.; Song, X. F. *J. Chem. Ind. Eng. (Chinese)* **2004**, *55*, 2032−2037.

(9) Zhang, Y. H.; She, Y. B.; Zhong, R. G.; Zhou, X. T.; Ji, H. B. *Acta Chim. Sin. (Chinese)*, **2004**, *62*, 2228−2232.

(10) Song, X. F.; Ji, H. B.; Zhou, X. T.; She, Y. B. *Fine Chem. (Chinese)* **2004**, *21* (6), 474−478.

10.1021/op049810b CCC: $30.25

Scheme 1



Central metal ions M: a. Co; b. Cu; c. Zn; d. Fe

Table 1. **Aerobic oxidation of *p*-nitrotoluene catalyzed by metal phthalocyanines**[a]

entry	catalyst	TON	*p*-nitrobenzoic acid yield (%)[b]
1	Ia	569	73.9
2	IIa	589	76.6[c]
3	Ib	556	72.3
4	IIb	570	74.1
5	Ic	549	71.1
6	IIc	569	74.0
7	Id	560	72.9
8	IId	549	71.3

[a] Reaction conditions: *p*-nitrotoluene (20 mmol), catalyst (0.13 mol %, based on the initial amount of *p*-nitrotoluene), methanol (50 mL), NaOH (120 mmol), oxygen (2.0 MPa), 12 h, 55 °C. [b] The isolated yield of *p*-nitrobenzoic acid. [c] Typical resulting mixture of reaction included 3.2% *p*-nitrobenzaldehyde, 7.8% *p*-nitrotoluene, and 1.2% *p*-nitrobenzyl alcohol by relative content with analysis of HPLC besides NaOH and the solvent.

acetic acid, was introduced into the oxidation as represented in Scheme 1, together with sodium hydroxide.

The oxidation reaction of *p*-nitrotoluene with 2.0 MPa of dioxygen at 55 °C was investigated with the above-mentioned metal phthalocyanines including Co, Cu, Zn, and Fe central metal ions as catalysts in NaOH−methanol solution, and the results are shown in Table 1.

It is encouraging that excellent catalytic performance of all metal phthalocyanines were shown from aerobic oxidation of *p*-nitrotoluene to *p*-nitrobenzoic acid with the respective isolated yields of product more than 70%, which is much higher than the best yield (less than 40%) reported by Chandalia and Mukhopadhyay.[2]

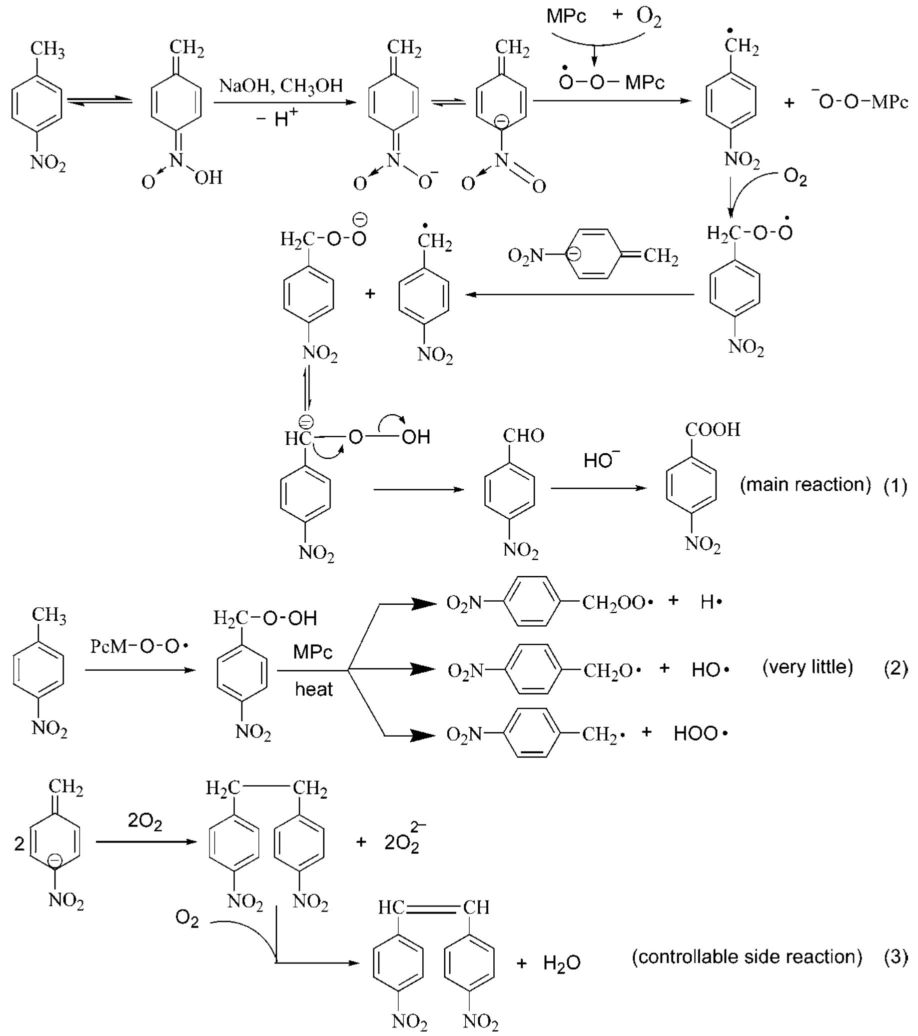
Note: There will be a potential hazard of explosion when using methanol, especially refluxing methanol, in a pure oxygen environment, although the explosion-limit range of methanol (6.0−36.5 vol %) is relatively narrower and the flash point of methanol (9 °C) is relatively higher than that of hydrocarbon solvents (<0 °C). Thus, much attention and careful designs must be given more than ever, considering the safety issues in industrial practice. For example, selecting the reaction temperature or O_2 pressure to be as low as possible will be completely out of the explosion-limit range of methanol (the fraction of methanol was 1.9−3.5 vol %, and methanol was not refluxed in the present process).

Furthermore, an electron-withdrawing substituent such as a carboxyl group was introduced into the phthalocyanine rings, and the effect on the catalytic performance of metal phthalocyanines was investigated, respectively. By comparison with those functionalized phthalocyanines, cobalt-, copper-, and zinc tetracarboxyl phthalocyanines exhibited an improved yield of *p*-nitrobenzoic acid (entries 1−6). However, for iron phthalocyanine catalyst, its functionalized iron tetracarboxyl phthalocyanine was less effective. To gain an insight into the reason, the solubility of metal phthalocyanines might be partly responsible for the yield enhancement, as the introduction of a carboxyl group into metal phthalocyanines increased their solubility in the NaOH−methanol solution in the order as cobalt > zinc > copper > iron, thus improving the probability between substrates and catalysts. Moreover, the introduced electron-withdrawing carboxyl groups enhanced the d orbital splitting energy of central metal ions, in turn, optimizing the electron configuration and changing the coplanarity of molecular planar structure, thus stabilizing those functionalized phthalocyanines and enabling few dimers, which obviously decreased its catalytic performance, formed among catalysts. Additionally, the delocalizing of the d orbit electrons increased the coordination capacity between central metal ions and substrate, which might explain the yield enhancement catalyzed by cobalt-, copper-, and zinc tetracarboxyl phthalocyanines.

The reason for the decreased performance of iron phthalocyanine could be found from the Jahn−Teller effect, i.e., according to crystal field theory. Octahedron structures of metal phthalocyanine complexes got deformed more or less with the exception of Zn^{2+} (d^{10}), and forming four short bonds was proved more stable than forming two short bonds; thus, the two poles of octahedron were generally elongated. Considering the metal phthalocyanines as above, first, for cobalt, the introduction of carboxyl group changed the d orbit energy level from $t_{2g}^{5}e_{g}^{2}$ to $t_{2g}^{6}e_{g}^{1}$, which will make the transition of an electron in e_g orbit to t_{2g} orbit, in turn, decreasing the electron cloud density of the *x*-*y* planar coordinate. As a result, its crystal field stabilization energy (CFSE) equaled $1.0\Delta_0$. Therefore, the phthalocyanine ring ligand was closer to the central Co^{2+}, and the shorter N−Co bonds favored the access of the substrate to the orienting Co^{2+} (entries 1, 2). However, for iron, the effect was unfavorable, as the introduction of the carboxyl group changed the electron configuration from $t_{2g}^{4}e_{g}^{2}$ to $t_{2g}^{6}e_{g}^{0}$, which was fully filled and fully blank, with its CFSE equaling to $2.0\Delta_0$; thus, the improved stabilization prevented the access of substrate and dioxygen to the central Fe^{2+} from two axis-oriented sides to some extent, and decreased its catalytic performance as a biomimetic catalyst (entries 7, 8). For copper and zinc, since no change occurred to Cu (d^9) $t_{2g}^{6}e_{g}^{3}$ and Zn (d^{10}) $t_{2g}^{6}e_{g}^{4}$, the electron-withdrawing carboxyl group contributed only to the increasing solubility of these catalysts.

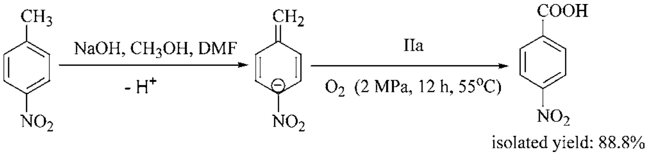
On the basis of literature and our earlier research work, the three possible mechanisms and paths of the above reaction could be described in eqs 1−3 of Scheme 2.

Scheme 2



According to our earlier research results,[11] the above three possible reactive paths in Scheme 2 could be effectively controlled by using suitable conditions. The research results showed that the above reaction only took place when a large amount of strong alkali such as NaOH−methanol existed in the reaction system; the yield of *p*-nitrobenzoic acid increased with the increasing NaOH concentration, and much less *p*-nitrobenzoic acid was obtained only where there was no NaOH in the reactive system. Obviously, eq 2 was not the main reactive path. Furthermore, the effects of the various reaction conditions on the yield of the target product were systemically investigated, which involved the initial concentration of *p*-nitrotoluene and NaOH, reaction temperature, dioxygen pressure, and the reaction time. The results showed that side reaction 3 could be completely controlled by adjusting the initial concentration of *p*-nitrotoluene and NaOH and selecting the proper temperature and oxygen pressure; byproducts such as 1,2-bis(4-nitrophenyl)ethane and 1,2-bis(4-nitrophenyl)ethylene were reduced dramatically, even null, under the recommended reaction conditions. Therefore, eq 1 should be the main path in the above basic liquid-phase medium, and side reactions in eq 3 hardly took place in optimum conditions. No other explosive byproducts such as dinitrobenzyls or dinitrosostilbene were detected through HPLC under the optimized reaction conditions.

Scheme 3



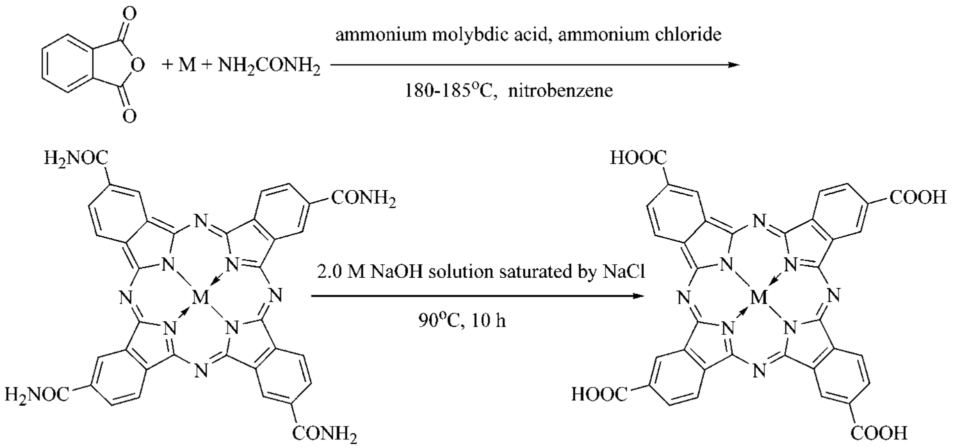
Further, it is strikingly surprising to find that a much better *p*-nitrobenzoic acid yield could be achieved via dissolving *p*-nitrotoluene into a small amount of dimethylformamide (DMF) before reaction, as shown in Scheme 3.

In comparison with the yield of 76.6% catalyzed by cobalt tetracarboxyl phthalocyanines without the addition of DMF before reaction, the addition of 2 mL of DMF contributed to the significant enhancement of the yield by about 12.2%, which made this process promising industrially. This 88.8% yield of *p*-nitrobenzoic acid was comparable with the yields of the following recent researches. For examples, Sawatari and coauthors[1] reported that oxidation of *p*-nitrotoluene under 1.0 MPa 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*-nitrobenzoic acid in 81% yield. Galstyan and

---

[11] She, Y. B.; Zhang, S. F.; Yang, J. Z. *J Dalian Univ. Technol. (Chinese)* **1999**, *39*, 56−59.

Scheme 4



coauthors[3−5] reported a closed process cycle by oxidation of *p*-nitrotoluene with an ozone−air mixture in the presence of $CoBr_2$ at 100 °C, and the best yield reached 96.6%; Chandalia and Mukhopadhyay[2] reported that less than 40% yield of *p*-nitrobenzoic acid, at 28 °C and 1.6 MPa air pressure, was achieved in 18 h using cobalt phthalocyanine. It should be noted that this present process has been relatively valuable in industry, as it uses a bromide-free and acetic acid-free reaction system in the presence of molecular oxygen at 55 °C.

Considering the effect of adding DMF, the addition of DMF improved the solubility of cobalt tetracarboxyl phthalocyanines and made it more dispersible in the system. On the other hand, since DMF was of strong polarity, the accessible tendency between cobalt ions and DMF prevented the dimerization of the phthalocyanine catalyst.

Conclusions

In conclusion, the isolated yield of *p*-nitrobenzoic acid catalyzed by cobalt tetracarboxyl phthalocyanine from the oxidation of *p*-nitrotoluene could be provided up to 88.8%, together with a small amount of dimethylformamide, under 2.0 MPa O_2 at 55 °C in the presence of molecular oxygen. Since methanol was not refluxed and the reaction temperature and O_2 pressure in the present process were so low, the partial pressure of methanol was out of its explosion-limit range. At the same time, no other explosive byproducts such as dinitrobenzyl or dinitrosostilbene were detected by HPLC under the optimized reaction conditions. The novel technology should be much safer than the conventional processes. Furthermore, the process was environmentally friendly, economical, and anticorrosive for equipment compared to the conventional methods, and the process should find practical application in industry.

In general, however, there might be certain potential hazards that should be paid more attention when a reaction was carried out in pure oxygen systems. It would be, of course, more preferable and safer if the pure oxygen were to be replaced with air or oxygen-rich nitrogen, and the reaction temperature and O_2 pressure were chosen to be as low as possible. The safer process and technology can be realized by some modification of the present novel technology for using air instead of dioxygen and adding a reflux condenser upon the autoclave to reflux solvent while releasing waste air during the reaction.

Experimental Section

Preparation of Metal Tetracarboxyl Phthalocyanine. The preparations of Co, Cu, Zn or Fe tetracarboxyl phthalocyanine were carried out in the same process, as shown in Scheme 4.

1. Cobalt Tetracarboxyl Phthalocyanine. To a 500-mL three-neckflask equipped with a magnetic stirrer and reflux condenser was added a mixture of trimellite anhydride (33.0 g, 187 mmol), $CoSO_4{\cdot}7H_2O$ (13.5 g, 50 mmol), NH_4Cl (4.5 g, 86 mmol), ammonium molybdic acid (0.5 g, 3 mmol), and sufficient finely ground urea in 35 mL of nitrobenzene; this resultant mixture was stirred for 3.5 h at 185 °C. The obtained mixture was then washed with methanol until no nitrobenzene could be detected, and a black-blue solid cobalt tetraformamido phthalocyanine was afforded. Followed by boiling about 3 min in the saturated sodium chloride solution and filtration, the filter cake was moved into 2.0 M NaOH solution saturated with NaCl in a 500-mL three-neck flask, and the reaction was performed at 90 °C for 10 h until no ammonia exited. The resulting solution diluted with appropriate amount of deioned water was brought to pH < 3 with concentrated hydrochloric acid; then centrifugation and filtration were executed, followed with dissolving well with 0.5 M NaOH solution and filtrating. After being repeated three times, the resulting solid was washed first with water and second with methanol until neutrality occurred. A claret solid with metallic luster (13.4 g, 34.8%) was obtained via drying in a vacuum. Anal. Calcd for $CoC_{36}H_{16}N_8O_8$: C, 57.8; H, 2.14; N, 14.99; Co, 7.90. Found: C, 57.8; H, 2.50; N, 15.12; Co, 7.50. Anal. HRMS (M^+): Calcd for $CoC_{36}H_{16}N_8O_8$, 747.0442; Found, 747.0442; *m/z* 747 $[M + H]^+$. IR(KBr) ν cm^{-1}: 3387.2, 1683.9, 1614.9, 1520.9, 1487.1, 1396.8, 1331.9, 1247.7, 1149.9, 1090.3, 944.0, 847.2, 779.4, 741.3, 644.4, 557.7, 484.3, 434.0.

2. Copper Tetracarboxyl Phthalocyanine. The same process as above was carried out except 12.0 g of $CuSO_4{\cdot}5H_2O$ was used instead of 13.5 g of $CoSO_4{\cdot}7H_2O$. 8.9 g, and a claret solid with metallic luster (8.9 g, 23.0%) was given. Anal. Calcd for $CuC_{36}H_{16}N_8O_8$: C, 57.45; H, 2.13; N, 14.89; Cu, 8.44; Found: C, 57.01; H, 2.54; N, 14.84;

Cu, 7.76. Anal. HRMS (M^+): Calcd for $CuC_{36}H_{16}N_8O_8$, Found, 752.0168; *m*/*z* 747 $[M + H]^+$. IR(KBr) ν cm^{-1}: 3354.2, 1659.0, 1613.4, 1574.4, 1506.0, 1384.2, 1327.1, 1245.9, 1147.3, 1087.5, 931.8, 845.4, 770.3, 736.6, 660.0, 549.0, 476.8, 430.0.

3. Zinc Tetracarboxyl Phthalocyanine. The same process as above was carried out except 6.5 g of $ZnCl_2$ was used instead of 13.5 g of $CoSO_4{\cdot}7H_2O$, and a bottle-green solid (1.2 g, 3.1%) was given. Anal. Calcd for $ZnC_{36}H_{16}N_8O_8$: C, 57.29; H, 2.12; N, 14.85; Zn, 8.67; Found: C, 57.01; H, 2.54; N, 14.84; Zn, 7.76. Anal. HRMS (M^+): Calcd for $ZnC_{36}H_{16}N_8O_8$, Found, 754.0481; *m*/*z* 747 $[M + H]^+$. IR (KBr) ν cm^{-1}: 3396.6, 1702.4, 1614.2, 1578.2, 1523.5, 1419.6, 1343.0, 1281.7, 1250.1, 1049.7, 928.2, 861.4, 832.2, 766.1, 739.8, 672.4.

4. Iron Tetracarboxyl Phthalocyanine. The same process as above was carried out except 9.5 g of $FeCl_2{\cdot}4H_2O$ was used instead of 13.5 g of $CoSO_4{\cdot}7H_2O$, and a blue-black solid (1.0 g, 13.0%) was given. Anal. Calcd for $FeC_{36}H_{16}N_8O_8$: C, 58.24; H, 2.16; N, 15.06; Fe, 7.51; Found: C, 58.48; H, 2.78; N, 15.52; Fe, 7.42. HRMS (M^+): Calcd for $FeC_{36}H_{16}N_8O_8$, Found, 744.0356; *m*/*z* 744 $[M + H]^+$. IR (KBr) ν cm^{-1}: 3339.3, 3181.7, 1660.6, 1611.5, 1576.8, 1513.3, 1383.9, 1328.6, 1250.2, 1150.0, 1088.0, 939.7, 850.0, 771.0, 741.0, 645.0, 432.7.

Preparation of Nitrobenzoic Acid from Oxidation of Nitrotoluene with Catalysis of Metal Phthalocyanines in the Presence of 2.0 MPa Dioxygen at 50 °C for 12 h. To a 200-mL autoclave was added 20 mmol of *p*-nitrotoluene with 50 mL of methanol and 120 mmol of NaOH as well as 0.13 mol % of the above synthesized metal phthalocyanines (based on the initial amount of *p*-nitrotoluene). The reaction was carried out for 12 h after 2.0 MPa dioxygen was introduced into the system, accompanied by magnetic stirrer stirring. When the reaction was finished, the reactor was allowed to cool to room temperature, and the pressure was released. The reaction mixture was filtered with the deionized water and acidified with hydrochloric acid to keep the pH less than 3.0. A white solid product was obtained (2.42−3.10 g) after filtration followed with drying.

Acknowledgment

We are indebted to the Key Project of the National Natural Science Foundation of China (No. 20436010), the Major Project of Science Foundation of Hunan University, the Science and Technology New Star project of Beijing Scientific Committee (No. 953811200), the Beijing Natural Science Foundation (No. 2002002), and the Youth Science Research Foundation of Beijing University of Technology (No. 00194) for financial support of this work.

Supporting Information Available

Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

Received for review October 14, 2004.

OP049810B