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N-Bridged Diiron Phthalocyanine Catalyzes Oxidation of Benzene with H_2O_2 via Benzene Oxide with NIH Shift Evidenced by Using 1,3,5-[D_3]Benzene as a Probe**

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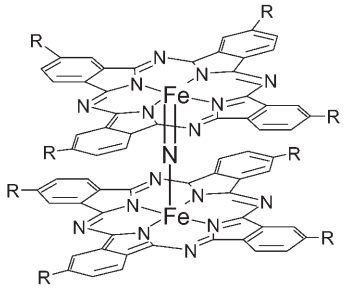
The ability of cytochromes P-450 and methane monooxygenases (MMO) to catalyse difficult oxidations of hydrocarbons have inspired numerous biomimetic studies. The progress in this challenging field deals with the development of metalloporphyrin-based systems[1] as well as mononuclear[2] and binuclear[3] iron non-heme complexes. Cytochrome P-450 chemistry involves mononuclear porphyrin complexes, while MMO chemistry is based on binuclear iron non-heme complexes. It should be noted that mimicking of the structural organisation and spectroscopic features of MMO has been achieved using diiron non-heme complexes, but no functional models able to oxidize methane have been published.[3a] One interesting possibility is to explore binuclear macrocyclic porphyrin-like complexes as oxidation catalysts. However, this approach has not yet been developed.

Our ongoing research is focused on developing clean oxidation processes using phthalocyanine complexes,[4,5] which are structurally relevant to porphyrins, but cheap and readily accessible on a large scale. Inspired by the observation that iron phthalocyanine supported in μ-oxo dimeric form (Fe-O-Fe motif) showed superior catalytic properties in the selective oxidation than monomeric FePc,[6] we have investigated catalytic properties of diiron phthalocyanines. N-Bridged binuclear complexes (metal-*N*-metal motif) constitute another family of dimers. Several μ-nitrido dimeric complexes with different ligands have previously been described.[7] To the best of our knowledge, these unusual complexes with interesting properties have never been used as oxidation catalysts. In particular, the unsubstituted $(FePc)_2N$ dimer, insoluble in organic solvents, contains Fe^{III}–N=Fe^{IV} fragment with one unpaired electron delocalized between two equivalent Fe sites with formal +3.5 state as was deduced from Mössbauer data ($\delta = 0.06\ mm\,s^{-1}$, $\Delta E_Q = 1.76\ mm\,s^{-1}$ at 77 K).[7b]

We have recently prepared an N-bridged diiron tetra-*tert*-butylphthalocyanine complex ($(FePc tBu_4)_2N$, Scheme 1),[8] which exhibits a good solubility in organic solvents and is more suitable for catalytic studies. This binuclear porphyrin-like complex with Fe-*N*-Fe structural unit interacts with H_2O_2, as shown by UV/Vis and EPR spectroscopies,[8] suggesting a possible activation of H_2O_2 to form oxidizing species. Indeed, we have recently shown that the active species derived from $(FePc tBu_4)_2N$ and H_2O_2 is able to perform an efficient oxidation of methane in water at ambient temperatures.[9] The $(FePc tBu_4)_2N$, characterized by different spectroscopic methods, retains its dimeric structure in the pres-



Scheme 1. μ-Nitrido-bridged iron tetra-*tert*-butylphthalocyanine, $(FePc tBu_4)_2N$, $R = C(CH_3)_3$.

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[**] NIH stands for National Institutes of Health where the shift was discovered.

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ence of H_2O_2.[9] ESI-MS experiments using $H_2{}^{16}O_2$ and $H_2{}^{18}O_2$ indicated the formation of a high valent diiron oxo complex $Fe^{IV}NFe^{V}$=O, which was proposed to be an active species responsible for oxidation of methane.[9] The mechanistic features of this binuclear complex are therefore of much interest.

To check the scope of this catalyst and to gain more information about catalytic properties of this unusual species, we have studied the oxidation of benzene, which is both industrially and biologically related process. Several enzymes, for example, cytochromes P-450, non-heme iron mono- and dioxygenases perform hydroxylation of aromatic compounds.[10,11] High valent iron oxo species were proposed to be involved in this demanding oxidation and arene oxide to be an obligatory intermediate in this reaction, although alternative pathways have also been proposed.[10] The main mechanistic hypotheses for benzene hydroxylation by cytochrome P-450 enzymes were carefully discussed by de Visser and Shaik.[12] Along with arene oxide, which could be formed from the tetrahedral intermediate oxo-iron–arene σ-complex, a characteristic feature of arene hydroxylation is the migration of the substituent from the hydroxylation site to the adjacent carbon position (NIH shift).[10] The mechanistic features of aromatic oxidation mediated by non-heme enzymes, in particular by toluene 4-monooxygenase,[11a] are quite similar to those of cytochrome P-450.[10] It is worth noting that the oxidation of benzene is less investigated in chemistry as compared to the oxidation of alkanes or olefins. Selective oxidation of benzene to phenol by N_2O was obtained over FeZSM-5 zeolite at 375 °C.[13] Titanium silicalite mediated the oxidation of PhH with H_2O_2.[14] FeAlPO catalysts were active in the oxidation of PhH by N_2O at 380 °C.[15] Low temperature oxidation of benzene usually associated with bio-inspired approach is, however, much less explored. Suicidal oxidation of the aromatic part of non-heme complexes was demonstrated,[16] but examples of oxidation of benzene are still rare. Non-heme iron polyazadentate complexes in combination with H_2O_2 and reducing agent oxidized benzene with TON ~8.[17]

Here we report on the mild oxidation of benzene and provide evidence that this oxidation occurs via formation of benzene oxide and involves the NIH shift thus resembling the biological aromatic oxidation. We have shown that 1,3,5-[D_3]benzene is a novel convenient probe for the detection of NIH shift.

$(FePc{t}Bu_4)_2N$ exhibited a high catalytic activity in oxidation of PhH by H_2O_2 even at 20 °C (Table 1). Phenol, the main oxidation product, was obtained with TON = 11. The efficiency of oxidation was increased at higher temperatures and higher concentration of PhH attaining TON_{PhOH} = 66. Three minor products were detected by GS-MS analysis. *p*-Benzoquinone was formed in minor quantity at 60 °C. Mass spectrum of second product (retention time = 4.0 min) corresponds to that published for benzene oxide (BO).[8,18] Mass spectra of this product derived from C_6H_6 (94 $[M]^+$, 78 $[M-O]^+$, 66 $[M-CO]^+$) and C_6D_6 (100 $[M]^+$, 84 $[M-O]^+$, 72 $[M-CO]^+$) differed on m/z 6 indicating the presence of all six H/D atoms on benzene core. The authentic benzene oxide was prepared according to published protocols.[19] The retention time and mass spectrum of the authentic BO and the product obtained in PhH oxidation were identical,[8] thus unambiguously proving the formation of benzene oxide in the course of PhH oxidation. Notably, when mononuclear $FePc{t}Bu_4$ or μ-oxo dimer $(FePc{t}Bu_4)_2O$ were used as catalysts at the same reaction conditions, the complete bleaching of the catalysts occurred within several minutes after H_2O_2 addition and no benzene oxide was detected in the reaction mixture.

The mass spectra of the other minor product (retention time = 9.25 min.)[8] with two oxygen atoms added to benzene core which were obtained from C_6H_6 (110 $[M]^+$, 81 $[M-CHO]^+$, 53 $[M-CHO-CO]^+$) and C_6D_6 (116 $[M]^+$, 86 $[M-CDO]^+$, 58 $[M-CDO-CO]^+$) matched to mass spectrum of *sym*-oxepin oxide.[19a] Molecular peaks of isotopomers of this product differ in m/z 6 indicating the presence of all H (D) atoms that is compatible with proposed oxepin oxide structure.

When 2% solution of $H_2{}^{18}O_2$ (Icon, >90% isotopic enrichment) in $H_2{}^{16}O$ was used for oxidation in the presence of $^{16}O_2$, phenol contained 93% of $Ph^{18}OH$, thus indicating that product oxygen was originated from $H_2{}^{18}O_2$. This finding strongly suggests that phenyl radical can not be an intermediate in this oxidation which would be trapped by $^{16}O_2$ leading to ^{16}O incorporation into phenol.

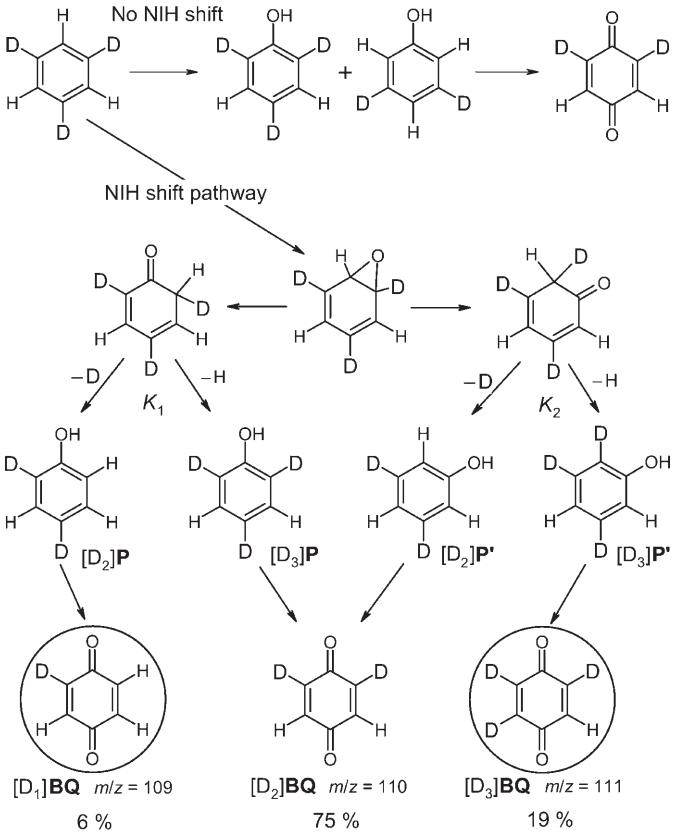
Intermolecular kinetic isotope effects (KIE) on phenol formation were determined using 1:1 C_6H_6/C_6D_6 mixture. At 25 °C and 60 °C KIEs were 1.21 ± 0.04 and 1.16 ± 0.02, respectively. Intramolecular KIE measured using 1,3,5-[D_3]benzene was 1.29 ± 0.03 at 25 °C. These KIE values are not compatible with the formation of σ-complex since in this case inverse KIE (<1) should be observed.[5g,10c,11a,12] The origin of the inverse KIE is a change in hybridization of hydroxylated carbon atom from sp^2 to sp^3 in the course of oxidation. According to the careful analysis of KIE associated with aromatic oxidation, k_H/k_D ~1.2 is compatible with reversible opening of the epoxide ring.[11a]

In addition to KIE determination, 1,3,5-[D_3]benzene is also a useful mechanistic probe to detect NIH shift. NIH shift is a migration of the substituent from the site of hydroxylation to adjacent carbon atom and usually associated with bio-oxidation.[10–12] The use of 1,3,5-[D_3]benzene as a NIH shift probe is based on the analysis of 1,4-benzoquinone (**BQ**) as indicated in Scheme 2. When no NIH shift occurs, **BQ** should contain only [D_2]**BQ. BQ** obtained from

Table 1. Oxidation of PhH by H_2O_2 catalyzed by $(FePc{t}Bu_4)_2N$.[a]

[PhH]/M	*T*/°C	*t*/h	Conversion/%	TON_{PhOH}
0.1	20	48	14	11
0.1	40	20	20	12
1	40	20	n.d.[b]	28
5.57	60	24	n.d.	66
11.14[c]	60	4	n.d.	32

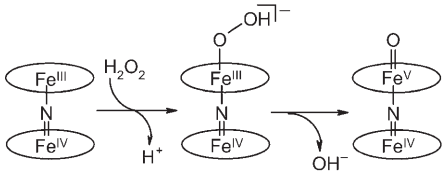
[a] Conditions: $[(FePc{t}Bu_4)_2N]=2.4\times10^{-4}$ M, $[H_2O_2]=0.22$ M in 2 mL MeCN. [b] n.d.: not determined. [c] Neat PhH.



Scheme 2. Proposed mechanism of oxidation of benzene by (FePc-*t*Bu$_4$)$_2$N–H_2O_2 system involving NIH shift.

$C_3D_3H_3$ contained 75% of [D_2]**BQ**, 19% of [D_3]**BQ** and 6% of [D_2]**BQ**, thus strongly suggesting NIH shift. A mechanism based on KIE and isotope labelling data is proposed in Scheme 2. **BO** formed in the first step undergoes to hydride (deuteride) shift to produce two 2,4-cyclohexadien-1-ones isotopomers $\mathbf{K_1}$ and $\mathbf{K_2}$, which enolize to phenols [D_2]**P**, [D_3]**P** and [D_2]**P′**, [D_3]**P′**, respectively, inducing NIH shift. These phenols can be oxidized to produce quinones [D_1]**BQ**, [D_2]**BQ** and [D_3]**BQ**. Importantly, [D_1]**BQ** and [D_3]**BQ** can be obtained only if NIH shift occurs in the course of oxidation. Thus, the analysis of isotopic composition of **BQ** can evidence NIH shift. **BQ** shows the clean molecular peak without $M-1$ and $M-2$ fragmentation and its isotopic composition can be calculated from mass spectrum.[8] The detection of [D_1]**BQ** and [D_3]**BQ** thus indicates the occurrence of NIH shift during oxidation of PhH by (FePc*t*Bu$_4$)$_2$N–H_2O_2 system.

The NIH shift and the formation of benzene oxide are usually associated with bio-oxidation mediated by cytochrome P-450 and toluene monooxygenases. In our previous paper describing the mild oxidation of methane,[9] we have proposed the formation of a high valent oxo-(FePc*t*Bu$_4$)$_2$N complex with two redox equivalents above $Fe^{III}NFe^{IV}$ state (Scheme 3). This proposal was based on the results obtained by UV/Vis, EPR, ESI-MS methods as well as in ^{18}O labelling experiments.[9] The proposed high valent Fe^{IV}-*N*-Fe^{V}=O species should be a very strong oxidant and thus be competent for the oxidation of such difficult-to-oxidize substrates as methane and benzene. The observation of the formation of benzene oxide and NIH shift in this work, which are characteristics of high valent iron oxo enzyme systems, is in agreement with proposed Fe^{IV}-*N*-Fe^{V}=O structure of active species. Fe^{IV}-*N*-Fe^{V}=O can be obtained *via* heterolytic cleavage of O−O bond in the putative Fe^{IV}-*N*-Fe^{III}-OOH hydroperoxo complex formed from (FePc*t*Bu$_4$)$_2$N and H_2O_2 (Scheme 3).



Scheme 3. Proposed mechanism of the formation of high valent diiron oxo species in (FePc*t*Bu$_4$)$_2$N–H_2O_2 system.

In sum, (FePc*t*Bu$_4$)$_2$N in combination with green and biologically relevant H_2O_2 shows a high activity in the mild oxidation of PhH. Turnover number based oh PhOH attains 66 cycles. Fe-*N*-Fe structural unit of μ-nitrido diiron complex is essential for this catalytic activity. Mononuclear FePc*t*Bu$_4$ and μ-oxo (FePc*t*Bu$_4$)$_2$O complex (Fe-O-Fe fragment) were rapidly destroyed and didn′t show the formation of benzene oxide during oxidation of benzene. Mechanistic features of benzene oxidation by (FePc*t*Bu$_4$)$_2$N–H_2O_2 system (formation of benzene oxide, NIH shift) are not compatible with free radical oxidation and resemble those of the biological oxidation, thus suggesting the involvement of high valent iron oxo species. NIH shift was evidenced using a novel mechanistic probe, 1,3,5-[D_3]benzene. To our knowledge, the formation of benzene oxide in course of the bio-inspired oxidation of benzene has been observed for the first time. The formation of benzene oxide is the two electron process typical for high valent oxo species.[1] ^{18}O labelling studies also suggest a possible involvement of a high valent oxo species. N-Bridged diiron phthalocyanine complexes show a new unexpected reactivity and provide a novel promising approach in the bio-inspired oxidation field.

Experimental Section

A 1:1 mixture of C_6D_6 and C_6H_6, 1,3,5-[D_3]benzene (98%, Aldrich) and 2% $H_2{}^{18}O_2$ in H_2O (90 atom%, Icon Isotopes) were used for the isotope labelling experiments. General procedure for catalytic oxidations: 40 μL of 35% H_2O_2 was added to 2.4×10^{-4} M (FePc*t*Bu$_4$)$_2$N in 2 mL of benzene solution in MeCN. The reaction mixture was stirred at desired temperature. The conversion of benzene and yield of phenol were determined by GC using external standard. The isotopic compositions of oxidation products were determined by GC-MS. Full details of the experimental procedures and instrumentation are given in the Supporting Information.

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Keywords: benzene · iron · phthalocyanine · oxidation

[1] a) B. Meunier, A. Robert, G. Pratviel, J. Bernadou in *The Porphyrin Handbook, Vol. 4* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, New York, **2000**, Chapter 31, pp. 119–187; b) J. L. McLain, J. Lee, J. T. Groves in *Biomimetic Oxidations Catalyzed by Transition Metal Complexes* (Ed.: B. Meunier), Imperial College Press, London, **2000**, pp. 91–169.

[2] a) M. Costas, M. P. Mehn, M. P. Jensen, L. Que, Jr., *Chem. Rev.* **2004**, *104*, 939–986; b) S. V. Kryatov, E. V. Rybak-Akimova, S. Schindler, *Chem. Rev.* **2005**, *105*, 2175–2226; c) M. Martinho, F. Banse, J. Sainton, C. Philouze, R. Guillot, G. Blain, P. Dorlet, S. Lecomte, J.-J. Girerd, *Inorg. Chem.* **2007**, *46*, 1709–1717.

[3] a) E. Y. Tshuva, S. J. Lippard, *Chem. Rev.* **2004**, *104*, 987–1012; b) A. Ghosh, F. T. de Oliveira, T. Yaho, T. Nishioka, E. S. Beach, I. Kinoshita, E. Münck, A. D. Ryabov, C. P. Horwitz, T. J. Collins, *J. Am. Chem. Soc.* **2005**, *127*, 2505–2513; G. Xue, D. Wang, R. De Hont, A. T. Fiedler, X. Shan, E. Münck, L. Que, Jr., *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 20713–20718.

[4] a) A. B. Sorokin, J.-L. Séris, B. Meunier, *Science* **1995**, *268*, 1163–1166; b) A. B. Sorokin, B. Meunier, *Chem. Eur. J.* **1996**, *2*, 1308–1317; c) A. B. Sorokin, S. De Suzzoni-Dezard, D. Poullain, J.-P. Noel, B. Meunier, *J. Am. Chem. Soc.* **1996**, *118*, 7410–7411.

[5] a) A. B. Sorokin, A. Tuel, *Catal. Today* **2000**, *57*, 45–59; b) C. Pérollier, A. B. Sorokin, *Chem. Commun.* **2002**, 1548–1549; c) S. L. Kachkarova-Sorokina, P. Gallezot, A. B. Sorokin, *Chem. Commun.* **2004**, 2844–2845; d) C. Pérollier, C. Pergrale-Mejean, A. B. Sorokin, *New J. Chem.* **2005**, *29*, 1400–1403; e) L. M. Gonzalez, A. L. Villa de P. , C. Montes de C. , A. B. Sorokin, *Tetrahedron Lett.* **2006**, *47*, 6465–6468; f) O. V. Zalomaeva, A. B. Sorokin, *New J. Chem.* **2006**, *30*, 1768–1773; g) A. B. Sorokin, B. Meunier, *Eur. J. Inorg. Chem.* **1998**, 1269–1281.

[6] A. B. Sorokin, S. Mangematin, C. Pergrale, *J. Mol. Catal. B* **2002**, *182–183*, 267–281.

[7] a) L. A. Bottomley, J.-N. Gorce, V. L. Goedken, C. Ercolani, *Inorg. Chem.* **1985**, *24*, 3733–3737; b) B. Floris, M. P. Donzello, C. Ercolani, in *Porphyrin Handbook, Vol. 18* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Elsevier Science, San Diego, **2003**, pp. 1–62.

[8] See the Supporting Information.

[9] A. B. Sorokin, E. V. Kudrik, D. Bouchu, *Chem. Commun.* **2008**, 2562–2564.

[10] a) P. R. Ortiz de Montellano, in *Cytochrome P-450: Structure, Mechanism and Biochemistry, 2nd ed.* (Ed.: P. R. Ortiz de Montellano), Plenum Press, New York, 1995, Chapter 8, pp. 245–303; b) B. Meunier, S. P. de Visser, S. Shaik, *Chem. Rev.* **2004**, *104*, 3947–3980; c) K. R. Korzekwa, D. C. Swinney, W. F. Trager, *Biochemistry* **1989**, *28*, 9019–9027; d) I. M. C. M. Rietjens, A. E. M. F. Soffers, C. Veeger, J. Vervoort, *Biochemistry* **1993**, *32*, 4801–4812.

[11] a) K. H. Mitchell, C. E. Rogge, T. Gierahn, B. G. Fox, *Proc. Natl. Acad. Sci. USA* **2003**, *100*, 3784–3789; b) P. F. Fitzpatrik, *Annu. Rev. Biochem.* **1999**, *68*, 355–381; F. P. Guengerich, *Chem. Res. Toxicol.* **2001**, *14*, 611–650.

[12] S. P. de Visser, S. Shaik, *J. Am. Chem. Soc.* **2003**, *125*, 7413–7424 and references therein.

[13] a) K. A. Dubkov, V. I. Sobolev, E. P. Talsi, M. A. Rodkin, N. H. Watkins, A. A. Shteinman, G. I. Panov, *J. Mol. Catal. A* **1997**, *123*, 155–161; b) V. S. Chernyavsky, L. V. Riruttko, A. K. Uriarte, A. S. Kharitonov, G. I. Panov, *J. Catal.* **2007**, *245*, 466–469 and references therein.

[14] a) D. Bianchi, L. Balducci, R. Bortolo, R. D′Aloisio, M. Ricci, G. Spanò, R. Tassinari, C. Tonini, R. Ungarelli, *Adv. Synth. Catal.* **2007**, *349*, 979–986; b) L. Balducci, D. Bianchi, R. Bortolo, R. D′Aloisio, M. Ricci, R. Tassinari, R. Ungarelli, *Angew. Chem.* **2003**, *115*, 5087–5090; *Angew. Chem. Int. Ed.* **2003**, *42*, 4937–4940.

[15] N. R. Shiju, S. Fiddy, O. Sonntag, M. Stockenhuber, G. Sankar, *Chem. Commun.* **2006**, 4955–4957.

[16] a) Y. Mekmouche, S. Menage, J. Pecaut, C. Lebrun, L. Reilly, V. Schuenemann, A. Trautwein, M. Fontecave, *Eur. J. Inorg. Chem.* **2004**, 3163–3171; b) F. Avenier, L. Dubois, J. M. Latour, *New J. Chem.* **2004**, *28*, 782–784.

[17] V. Balland, D. Mathieu, N. Pons-Y-Moll, J. F. Bartoli, F. Banse, P. Battioni, J.-J. Girerd, D. Mansuy, *J. Mol. Catal. A* **2004**, *215*, 81–87.

[18] G. R. Gillard, M. J. Newlands, J. N. Bridson, D. J. Burnell, *Can. J. Chem.* **1991**, *69*, 1337–1343.

[19] a) W. H. Rastetter, *J. Am. Chem. Soc.* **1976**, *98*, 6350–6353; b) S. G. Davies, M. E. C. Polywka, S. E. Thomas, *J. Chem. Soc. Perkin Trans. 1* **1986**, 1277–1282.

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