Hydroxylation of Hexane Using Dioxygen and Trimethylhydroquinone: Biomimetic Catalysis by an Unsymmetrical Diiron-μ-Oxo Complex

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An unusual unsymmetrical diiron(III) complex has been obtained with an amine/pyridine ligand. Its ability to catalyze the hydroxylation of *n*-hexane with O_2 and trimethylhydroquinone as reductant and proton donor, respectively, is reported in homogeneous and supported conditions. A spectroscopic study is reported to confirm the role of the reductant. A high-valent iron-oxo species is suggested.

Introduction

Transforming alkanes into alcohols under environmentally friendly conditions (i.e. using O_2 at room temperature) is a challenge for chemists.[1] In the area of biomimetic chemistry, complexes with porphyrins[2] or amine/pyridine ligands[3] are extensively used to model the active site of mono- or dinuclear iron-containing biological systems capable of performing the above-mentioned reaction. Among nonheme metallobiomolecules able to hydroxylate a CH bond using O_2 and electrons, one can evoke two systems: the antitumoral drug Bleomycin (BLM),[4,5] which cleaves DNA oxidatively, or the metalloenzyme methane monooxygenase (MMO),[6,7] which catalyzes the conversion of methane into methanol. In both cases, the entity responsible for the oxidation of the CH bonds has been suggested to be a high valent iron-oxo compound. In the case of MMO, the active state is an $Fe^{IV}(\mu\text{-}O)_2Fe^{IV}$ intermediate (compound Q) derived from the peroxo form Fe^{III}(μ-1,2-peroxo)Fe^{III} (compound P). It has been envisioned that the so-called "activated BLM" Fe^{III}-OOH dissociates to yield $Fe^{IV}O + OH^{\cdot}$ or $Fe^{V}O + OH^{-}$.

Most of the synthetic models that mimic the oxidation reactions catalyzed by these natural systems do not react directly with O_2 plus a reductant, but with H_2O_2 instead.[3] Although some peroxo models have been obtained by reacting Fe^{II} complexes with O_2,[8,9] only a few complexes have been reported to catalyze alkane oxidation reactions with dioxygen as oxidant.[3,10] In this communication, we report a new unsymmetrical dinuclear Fe^{III} complex obtained with the ligand *N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)propane-1,3-diamine (L_4^3). This diiron(III) complex can be reduced to the Fe^{II} state to further react with dioxygen and converts *n*-hexane into *n*-hexanols.

Results and Discussion

The molecular structure of $[L_4^3Fe^{III}(Cl)(\mu\text{-}O)Fe^{III}Cl_3]$ (**1**) has been resolved by X-ray diffraction (cf. Figure 1).[11] The structure can be described as two different units bridged by an oxo group. The first unit is an iron center in a pseudo-octahedral environment with the L_4^3 ligand wrapping around the metal in a *cis*-β fashion; a chloro ligand and the oxo bridge complete the coordination sphere. The second unit is an Fe^{III} moiety in a tetrahedral environment with three chloro ligands and the oxo bridge. Very few examples of this type of unsymmetrical dinuclear Fe^{III} complexes have been described.[12−15] Moreover the complex described here is the first one which has been obtained with pyridine groups.

Although the possibility that the unsymmetrical diiron units can be considered as models for biological systems has been envisioned,[12−15] no reactivity studies have been carried out with these complexes. The catalytic activity of **1** towards oxidation of *n*-hexane with molecular dioxygen has been evaluated in the presence of acetic acid and trimethylhydroquinone as reductant. At the beginning of the reaction the solution is purple, although this color disappears after about 10 minutes. The results were monitored period-

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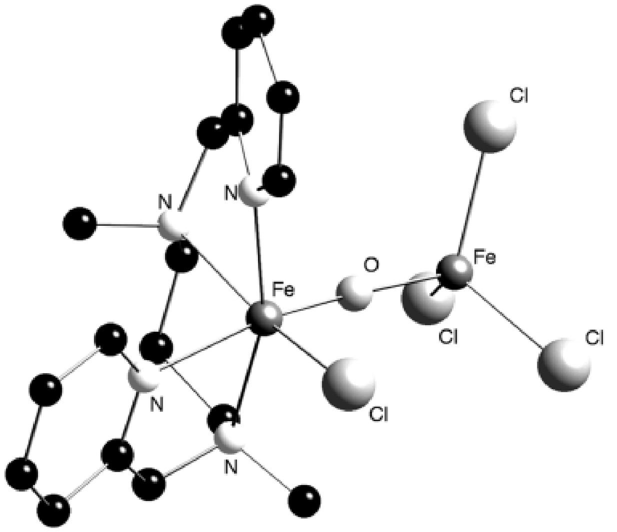

Figure 1. Molecular structure of [L$^3_4$Fe^{III}(Cl)(μ-O)Fe^{III}Cl$_3$] (**1**)

ically by GC and those recorded after 2 and 16 hours are gathered in Table 1. The total number of turnovers (ca. 10) is reached after 2 hours and further reaction time does not increase the yield nor alter the distribution of the products. Separate experiments confirmed that the presence of **1** in the reaction mixture was necessary for the oxidation of the substrate. Very interestingly, the alcohol-to-ketone ratio is much higher than 1. Such a high ratio is indicative of the absence of radical chain autoxidation, thereby suggesting the involvement of a metal-centered oxidation.[3] The evolution of this ratio from 15.5 to 50 when the reaction time increases seems artificial. Indeed, the yield of ketones decreases slightly while the yield in alcohols increases. As this phenomenon concerns a low number of turnovers, it is probably the consequence of side reactions, for example, reduction of the ketones by the excess reductant. Moreover, these side reactions take place over a period much longer than the time necessary to reach the total number of turnovers; they are therefore too slow to be responsible for the high A/K ratio observed after 2 hours.

Table 1. Oxidation of *n*-hexane by O_2 with by catalyst/trimethylhydroquinone/acetic acid[a]

System (duration)	Products (T.N.)					TTN[b]	A/K[c]
	1-ol	2-ol	3-ol	2-one	3-one		
1 in solution (2 h)	1.0	3.4	4.9	0.3	0.3	9.9	15.5
1 in solution (16 h)	1.1	3.7	5.2	0.1	0.1	10.2	50
1 on silica (2 h)	0.2	1.0	1.3	0.5	0.5	3.5	2.5
1 on silica (16 h)	5.1	17.8	22.2	1.9	2.1	49.1	11.3

[a] Yields are given as turnover numbers (T.N.) based on **1**. Reaction conditions: 1 atm. O_2 at 25 °C in 2.6 mL of dry acetonitrile; final concentration for the catalyst in the reaction mixture 0.33 mmol·L^{-1}. catalyst/*n*-hexane/trimethylhydroquinone/acetic acid 1:3000:350:250. [b] TTN stands for total number of turnovers. [c] Alcohols/ketones ratio.

Concerning the total number of turnovers and the A/K ratio, the results listed in Table 1 are of the same order as those reported for the oxidation of cyclohexane and *n*-pentane catalyzed by [{Fe(HBpz$_3$)(hfacac)}$_2$O].[16] The same experiments were carried out without any acetic acid: the same product distribution was observed but the total yield was reduced by a factor of three. This suggests that maintaining a dimeric structure for the catalyst by means of an acetate bridge increases the lifetime of the catalyst **1**. We are currently trying to isolate the species that forms in the presence of acetate. Recently, White et al. made similar observations: they used acetate to increase the product yield and robustness of their catalyst.[17]

The same conclusion is suggested by the results obtained in heterogeneous conditions.(cf. Table 1). Upon immobilizing the L$^3_4$ ligand on a silica support,[18,19] the yield is increased by a factor of five after 16 hours. Contrary to the experiments in solution, these results improve drastically with time. This is not surprising if one considers that the substrate has to reach the metal center and the product has to be removed in solution before analysis. The reactivity has also been explored under slightly different conditions (results not reported in Table 1). This allows us to determine the following: i) as under homogeneous conditions, acetic acid increases the yield; ii) when the silica support was not treated with the C-18 chain (see figure in Supporting Information), the yield decreased. It appears that a hydrophobic matrix facilitates the reactivity. One can propose that, because of the long alkyl chains, the hydrophobic substrate is driven to the reactive site and the polar products are easily eliminated; iii) whatever the conditions, the heterogeneous catalyst was always more efficient than the homogeneous one for a reaction time of 16 hours.

In order to propose a mechanism for the catalytic oxidation of *n*-hexane by O_2 in the presence of trimethylhydroquinone and **1**, we have studied the reaction between **1** and the reductant in the absence of any substrate. The evolution as a function of time of a solution of equimolar amounts of **1** and trimethylhydroquinone (TMH$_2$Q) in acetonitrile under argon has been followed by UV/Visible spectroscopy (Figure 2). The characteristic LMCT bands of the unsymmetrical dimer **1** at 347 nm and 420 nm[20] decrease in intensity as the reaction evolves. At the same time the characteristic bands of trimethylquinone at 255 and 266 nm appear. No further change is observed after one hour. However, if dioxygen is gently bubbled through the reaction mixture for three days, the electronic spectrum reveals that the dinuclear compound **1** partly reforms (see Figure 2). With a TMH$_2$Q/**1** ratio of 1:1 the reoxidation by O_2 is slow. However, when using a much larger amount of reductant relative to **1**, we observed that this redox process becomes cyclic — and much faster (ca. 1 minute for each cycle) — by degassing or oxygenating the solution. It is most likely that in the presence of an excess of TMH$_2$Q, an Fe^{III}-TMHQ complex is formed, as indicated by the purple color (λ_{max} = 568 nm) attributed to a charge transfer between a phenolato group and Fe^{III}.[21,22] The Fe^{II}-trimethylhydroquinone complex then formed is reoxidized by O_2 much

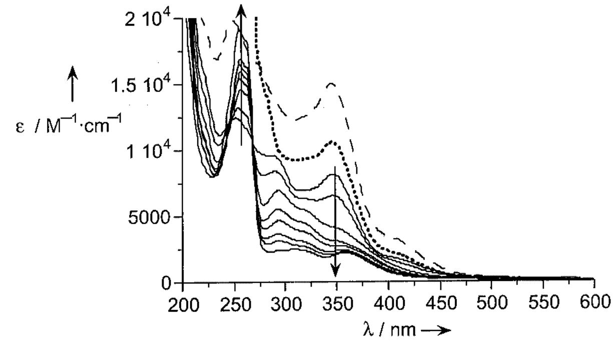

Figure 2. UV/Vis spectra of: (a) **1** + 1 equiv. of trimethylhydroquinone under argon (full line); (b) spectrum obtained after three days under O_2 at the end of evolution (a) (dotted line); spectrum of $L^3_4Fe^{III}(Cl)(\mu\text{-}O)Fe^{III}Cl_3$ **1** (dashed line)

more rapidly than the Fe^{II}-Cl complexes in the above experiment. Thus it appears that TMH_2Q plays a double role in the catalysis: reduction of Fe^{III} and displacement of the chloro ligands to give a Fe^{II}-trimethylhydroquinone complex that is more sensitive to O_2. The importance of ligation of hydroquinones to iron has already been pointed out.[23]

The observations reported above are in agreement with a mechanism implying a high-valent iron species: initial reduction of the dinuclear Fe^{III}-oxo complex **1** by trimethylhydroquinone to the Fe^{II} level allows dioxygen to interact with the metal centers to finally yield a high valent iron-oxo entity. However some questions remain to be elucidated, in particular the chemical nature (mono- or dinuclear) of the active species has to be addressed.

Conclusion

Compared to synthetic models, the pre-eminence of enzymatic systems resides in the separation of the successive steps in the catalytic cycle, whereas for model systems all the reactants are mixed together. The crucial reaction, i.e. oxidation of *n*-hexane by a putative mono- or dinuclear Fe^{IV} species, is in competition with oxidation of the excess reductant. The challenge for chemists in the coming years is therefore to devise catalytic systems in which the different steps can be timely orchestrated.

Experimental Section

The ligand L^3_4 was prepared following the method reported for the ligand bispicen[24] but using *N,N′* dimethyl-1,3-propane diamine as starting material.

Synthesis of 1: A 7 mL methanolic solution of $FeCl_3{\cdot}6H_2O$ (165 mg, 0.61 mmol) was added to a solution of L^3_4 (1 equiv., 173 mg) in 10 mL of MeOH. The solution was stirred for a few minutes and a dark orange powder precipitated. The solid was filtered and washed twice with methanol (174 mg, 50%). Crystals were obtained within a few hours by diffusion of *tert*-butyl methyl ether into a solution of **1** in acetonitrile. $C_{17}H_{24}Cl_4Fe_2N_4O{\cdot}1/2CH_3OH$ (569.92 g·mol^{-1}): calcd. C 36.88, H 4.60, Cl 24.88, Fe 19.60, N 9.83; found C 36.74, H 4.50, Cl 24.77, Fe 19.34, N 9.74.

Syntheses of the grafted ligand and supported catalyst are available as Supporting information(see footnote on the first page of this article).

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[1] J. M. Thomas, R. Raja, G. Sankar, R. G. Bell, *Acc. Chem. Res.* **2001**, *34*, 191.

[2] B. Meunier, A. Robert, G. Pratviel, J. Bernardou, in *The Porphyrin Handbook, Vol. 4* (Eds.: K. M. Kadish, K. Smith, E. R. Guilard), Academic Press, San Diego, **2000**, p. 119.

[3] M. Costas, K. Chen, L. Que, *Coord. Chem. Rev.* **2000**, *200−202*, 517.

[4] J. Stubbe, J. W. Kozarich, W. Wu, D. E. Vanderwall, *Acc. Chem. Res.* **1996**, *29*, 322.

[5] R. M. Burger, *Chem. Rev.* **1998**, *98*, 1153.

[6] B. J. Wallar, J. D. Lipscomb, *Chem. Rev.* **1996**, *96*, 2625.

[7] M. Merkx, D. A. Kopp, M. H. Sazinsky, J. L. Blazyk, J. Müller, S. J. Lippard, *Angew. Chem. Int. Ed.* **2001**, *40*, 2782.

[8] J. DuBois, T. J. Mizoguchi, S. J. Lippard, *Coord. Chem. Rev.* **2000**, *200−202*, 443.

[9] S. V. Kryatov, E. V. Rybak-Akimova, V. L. MacMurdo, L. Que, *Inorg. Chem.* **2001**, *40*, 2220.

[10] T. Funabiki, T. Toyoda, S. Yoshida, *Chem. Lett.* **1992**, 1279.

[11] Crystal data for **1**: $C_{17}H_{24}Cl_4Fe_2N_4O_1$, $M_w = 553.90$. Crystal dimensions 0.15 × 0.12 × 0.10. The data were collected at 123 K on a Nonius Kappa-CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation. The structures were solved by direct methods with SHELXS-97 and refined by full-matrix least-squares on F^2 with anisotropic thermal parameters for all non-H atoms with SHELXL-97. Triclinic, space group $P\bar{1}$, $a = 9.6360(19)$, $b = 15.151(3)$, $c = 17.665(4)$ Å; $\alpha = 114.77(3)$, $\beta = 100.65(3)$, $\gamma = 90.01(3)$; $V = 2292.6(8)$ Å^3; $Z = 4$. 12065 measured reflections, of which 6879 were unique. CCDC-171973 contains the complete supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

[12] P. Gomez-Romero, G. C. DeFotis, G. B. Jameson, *J. Am. Chem. Soc.* **1986**, *108*, 851.

[13] P. Gómez-Romero, E. H. Witten, W. M. Reiff, G. Backes, J. Sanders-Loehr, G. B. Jameson, *J. Am. Chem. Soc.* **1989**, *111*, 9039.

[14] P. Gómez-Romero, E. H. Witten, W. M. Reiff, G. B. Jameson, *Inorg. Chem.* **1990**, *29*, 5211.

[15] J. Wang, M. S. Mashuta, Z. Sun, J. F. Richardson, D. N. Hendrickson, R. M. Buchanan, *Inorg. Chem.* **1996**, *35*, 6642.

[16] N. Kitajima, M. Ito, H. Fukui, Y. Moro-oka, *J. Chem. Soc., Chem. Commun.* **1991**, 102.

[17] M. C. White, A. G. Doyle, E. N. Jacobsen, *J. Am. Chem. Soc.* **2001**, *123*, 7194.

[18] K. Miki, T. Furuya, *Chem. Commun.* **1998**, 97.

[19] D. Brunel, N. Bellocq, P. Sutra, A. Cauvel, M. Laspéras, P. Moreau, F. DiRenzo, A. Galarneau, F. Fajula, *Coord. Chem. Rev.* **1998**, *178–180*, 1085.

[20] N. Raffard, F. Banse, E. Anxolabehere-Mallart, M. Nierlich, J.-J. Girerd, *Inorg. Chem.* to be submitted.

[21] P. Mialane, E. Anxolabéhère-Mallart, G. Blondin, A. Nivorojkine, J. Guilhem, L. Tchertanova, M. Césario, N. Ravi, E. Bominaar, J.-J. Girerd, E. Münck, *Inorg. Chim. Acta* **1997**, *263*, 367.

[22] B. Adam, E. Bill, E. Bothe, B. Goerdt, G. Haselhorst, P. Hildebrandt, A. Sokolowski, S. Stenken, T. Weyermüller, K. Wiegardt, *Chem. Eur. J.* **1997**, *3*, 308.

[23] T. Funabiki, T. Yokomizo, S. Suzuki, S. Yoshida, *Chem. Commun.* **1997**, 151.

[24] H. A. Goodwin, F. Lions, *J. Am. Chem. Soc.* **1960**, *82*, 5013.

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