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μ-oxo Diferric Complexes as Oxidation Catalysts with Hydrogen Peroxide and their Potential in Asymmetric Oxidation

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Abstract : Non-heme diiron complexes, as models of methane monooxygenase, provide a new class of catalysts for oxidation reactions. We show here that such complexes have the potential for catalyzing stereoselective oxidations of sulfides by hydrogen peroxide. © 1997 Elsevier Science Ltd.

Catalytic asymmetric oxidation of sulfides has met with success in a few cases. Active systems described so far are based on titanium-binaphtol,[1] titanium-tartrate,[2] Mn-salen catalysts[3] and vanadium-based catalysts.[4] Asymmetric sulfoxidation with an iron catalyst has been reported only in the case of chiral iron porphyrins but enantioselectivity was moderate.[5] In all cases, oxidants used were alkylhydroperoxides or iodosylbenzene (PhIO).[6]

Since non-heme diiron complexes, as models for the diiron site of methane monooxygenase[7] were recently shown to represent a new class of catalysts for oxidation reactions in organic solvents,[8-11] we explored their potential for asymmetric oxidation of sulfides. In this report, we describe the first highly robust non-heme iron complex with a significant ability to catalyze asymmetric oxidation of sulfides by hydrogen peroxide. The new complex, compound **1**, $Fe_2O(L)_4(H_2O)_2(ClO_4)_4$,[12] is an extension of our best previously reported bipyridine-based iron catalyst,[13] as it contains a bipyridine (bipy) ligand in which a chiral substituent (L = (-)4,5 pinene bipyridine),[14] has been introduced (figure 1).

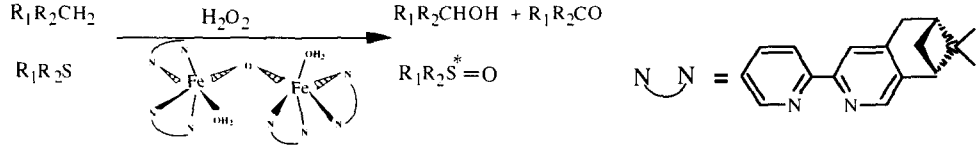

Figure 1

Table 1 shows that the new complex displays catalytic activities for the oxidation of cyclohexane, ethylbenzene, 1-phenylethanol, cyclooctene and dimethylsulfide at room temperature. The reactions are fast as they are completed after less than 10 minutes (20 catalytic cycles per min in the case of dimethylsulfide) at room temperature. The optimal yields presented here, which are the largest among reported values for oxygenations of alkanes and sulfides by H_2O_2 with this class of diiron catalysts, were obtained when H_2O_2 was slowly added to the reaction mixture. A low concentration of the peroxide is required to limit its Fe-catalyzed dismutation. For example, in the case of cyclohexane oxidation (substrate:H_2O_2:**1** = 1100:100:1) cyclohexanol and cyclohexanone were produced with an overall reaction yield of 40%, compared to a yield of 15% when H_2O_2 was added as one

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single injection. This has been also observed previously with TBHP (t-butylhydroperoxide) as the oxidant in similar systems based on diiron complexes.[15,16]

Not shown here is also the interesting observation that, in all cases, complex **1** was recovered intact and its catalytic activity remained constant after multiple turnovers (at least 50 catalytic cycles) proving its great robustness. In comparison the analog complex $Fe_2O(bipy)_4(H_2O)_2(ClO_4)_4$ was rapidly inactivated during catalysis, mainly due to conversion to the mononuclear inactive ferrous complex $[Fe(bipy)_3]^{2+}$.[13] It would be interesting to understand the molecular basis for the greater stability of complex **1**.

Table 1 : Oxidations of Various Substrates by H_2O_2 (25 equiv.) Catalyzed by complex **1**[(a)]

Substrate	Products	T .N [(b)]	Yield(%)[(c)]
cyclohexane	cyclohexanol cyclohexanone	5 2.5	40
ethylbenzene	1-phenylethanol acetophenone	6.5 7	82
1-phenylethanol	acetophenone	4	20
cyclooctene	cyclooctene oxide	9	36
dimethylsulfide[(d)]	dimethylsulfoxide	20	78

a) experimental conditions: reactions were carried out in acetonitrile under argon using 0.7 mM catalyst, 25 equivalents H_2O_2 in five successive portions and either 1100 equivalents of alkanes or alkene, 20 equivalents of alcohol or 600 equivalents of sulfide. After 10 minutes (or 5 minutes in the case of sulfide oxidation) products were analyzed by GC. b) T.N: turnover number in mmol of products/ mmol of catalyst. c) yields are based on the limiting reactant: H_2O_2 for all cases except for alcohol oxidation. In the case of alkane oxidation, the yield takes into account the fact that two equiv. of oxidant are required to make one equiv. of ketone. d) no dimethylsulfone could be detected.

As shown in table 2, complex **1** was able to catalyze asymmetric oxidations of sulfides by H_2O_2, with excellent yields. It is interesting to note that the oxidation reaction gave exclusively sulfoxides (no sulfones). For a comparison, very little sulfoxidation, less than one turn-over, was obtained when TBHP was used as the oxidant. The observed enantioselectivity was moderate but significant with an enantiomeric excess of 38 % in the case of p-bromo(phenyl)methylsulfide.[17] In all cases, the R enantiomer was the major product. The enantiomeric excess decreased with increased H_2O_2 concentration added in a single injection but was not affected by the presence of dioxygen. As control experiments, we showed that both $Fe_2O(bipy)_4(H_2O)_2(ClO_4)_4$/ H_2O_2 and complex **1**/TBHP systems generated only a racemic mixture of the sulfoxides (ee = 0%). In the absence of the catalyst, no oxidation occurred. This was also the case when the chiral ligand alone was present in place of complex **1**.

We have thus described the first catalytic system using a simple and robust non-heme diiron catalyst and hydrogen peroxide able to oxidize sulfides to sulfoxides with significant enantiomeric excesses,[18] excellent reaction yields and turnover frequency. Certainly, the enantioselectivity of the present system is far from that of

systems based on Ti or Mn(salen) catalysts. However, it is comparable to that of systems based on chiral iron porphyrins.

Furthermore, in contrast to previously reported catalytic systems including those based on diiron complexes of the same class as complex **1**, the oxidant used here is not an alkylhydroperoxide, a peracid or iodosylbenzene but instead hydrogen peroxide, a much cheaper and cleaner oxidant (water is the only by-product) with more future for synthetic or industrial applications. Complex **1** proved to be relatively more efficient for oxidation reactions than for dismutation of H_2O_2.

Finally, our results provide the first direct evidence that oxidation reactions catalyzed by non-heme iron do not proceed exclusively through radical chain autoxidation as it is generally accepted.[19] Under certain conditions, metal-based pathways in which the oxygen active species is bound to the metal may be involved, thus allowing some control of the stereoselectivity of the reactions, as earlier proposed by Groves et al.[20] and more recently by Que et al.[15] and ourselves. [21] A mononuclear chiral bleomycin-iron complex was also shown to catalyze the stereoselective epoxidation of alkenes by H_2O_2.[22]

Even though the molecular basis for the stereoselective oxidation of sulfides reported here remains to be established, we are convinced that further improvement of chiral non-heme diiron catalysts is a realistic and promising challenge.

Table 2 : Oxidation of prochiral Sulfides by Hydrogen Peroxide Catalyzed by Complex **1.**

substrate[a]	confign.	temperature(°C)	ee (%)	yield (%)[b]
thioanisole	R-(+)	r.t.	18	90
	R-(+)	-15	21	100
p-tolylmethylsulfide	R-(+)	-15	28	68
p-bromo(phenyl)methylsulfide	R-(+)	-15	40	90

a) Experimental conditions: 0.7 mM of complex **1**, 600 equivalents of sulfides were degassed before addition of 10 equivalents of hydrogen peroxide. b)yields based on the oxidant after 10 minutes reaction.

References and Notes.

1. Komatsu, N.; Hashizume, M.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 4529-4533.
2. Brunel, J. M.; Kagan, H. B. *Synlett* **1996**, 404-406 and references therein.
3. Kokubo, C.; Katsuki, T. *Tetrahedron* **1996**, *52*, 13895-13900.
4. Bolm, C.; Bienewald, F. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2640-2642.
5. Groves, J. T.; Viski, P. *J. Am. Chem. Soc.* **1989**, *111*, 8537-8539.
6. (a) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628-3634.(b) Naruta, Y. ; Tani, F.; Maruyama, K. *Tetrahedron: Asymmetry* **1991**, *2*, 533-542.

7. (a) Rosenweig, A. C.; Frederick, C. A.; Lippard, S. J.; Nordlund, P. *Nature* **1993**, *366*, 537-543. (b) Green, J.; Dalton, H. *J. Biol. Chem.* **1989**, *264*, 17698-17703. (c) Andersson, K. K.; Froland, W. A.; Lee, S. K.; Lipscomb, J. D. *New. J. Chem.* **1991**, *15*, 411-415.
8. (a) Fish, R. H.; Konings, M. S.; Oberhausen, K. J.; Fong, R. H. ; Yu, W. M.; Christou, G.; Vincent, J. B.; Coggin, D. K.; Buchanan, R. M. *Inorg. Chem.* **1991**, *30*, 3002-3006. (b) Barton, D. H. R.; Bévière, S. D.; Chavasiri, W.; Csuhai, E.; Doller, D.; Liu, W.-G. *J. Am. Chem. Soc.* **1992**, *114*, 2147-2156. (c) Gritsenko, O. N.; Nesterenko, G. N.; Shteinman, A. *Russian Chemical Bulletin*, **1995**, *44*, 2415-2417.
9. Leising, R. A.; Kim, J.; Perez, M. A.; Que Jr. ,L. *J. Am. Chem. Soc.* **1993**, *115*, 9524-9530.
10. a) Ménage, S.; Vincent, J.-M.; Lambeaux, C.; Chottard, G.; Grand, A.; Fontecave, M. *Inorg. Chem.* **1993**, *32*, 4766-4773. b) Ménage, S.; Galey, J.B.; Hussler, G.; Seité, M.; Fontecave, M. *Angew. Chem. Int. Ed. Engl.* **1996**. *35*, 2353.
11. Kodera, M.; Shimakoshi, H.; Kano, K. *J. Chem. Soc. Chem. Comm.*, **1996**, 1737-1738.
12. Complex **1** was synthesized by mixing 1 equivalent of $Fe(ClO_4)_3 \cdot 9H_2O$ and 2 equivalents of L in ethanol to afford a green solid. Anal.Calcd. For $\mathbf{1} \cdot 4H_2O \cdot EtOH$ ($C_{70}H_{88}Cl_4Fe_2N_8O_{23}$): C, 50.03; H, 5.36; Cl, 8.45; Fe, 6.60; N, 6.60. Found: C, 49.95; H, 5.32; Cl, 8.90; Fe, 6.35; N, 6.29. UV-vis [CH_3CN, λ_{max}, ε]: 610 nm (160 $M^{-1}.cm^{-1}$), 460 (sh, 1000), 350 (10000). ^1H NMR (CD_3CN, 200 MHz) δ in ppm : 25.3 ($H_\alpha$py), 18.7, 16.4, 14.6, 12.8 ($H_\beta$py), 8.3 and 7.7 ($H_\gamma$py). Protons of the pinene moities spread out between 3 and 1 ppm. Complex **1** is EPR silent. All the spectroscopic characteristics are similar to those of $Fe_2O(bipy)_4(H_2O)_2(ClO_4)_4$ (see ref. 10).
13. Ménage, S; Vincent, J.-M.; Lambeaux, C.; Fontecave, M. *J. Chem. Soc. Dalton Trans.* **1994**, 2081-2084.
14. Hayoz, P.; von Zelewsky, A.; Stoeckli-Evans, H. *J. Am. Chem. Soc.* **1993**, *115*, 5111-5114.
15. Kim, J.; Harrison, R. G.; Kim, C.; Que Jr.; L. *J. Am. Chem. Soc.* **1996**, *118*, 4373-4377.
16. Toia, C.; Ménage, S.; Lambeaux, C.; Fontecave, M. unpublished result.
17. Optical yields were measured by ^1H NMR using a chiral shift reagent, *R*- 2,2'dihydroxy1,1'binaphtyl (see reference : Toda, F.; Mori, K.; Okada, J. ; Node, M.; Itoh, A.; Oomine, K.; Fuji, K. *Chem. Let.* **1988**, 131-134) and confirmed by polarimetry .
18. During oxidation of ethylbenzene, a small but reproducible excess of the R enantiomer of 1-phenylethanol (ee=5%) was obtained. Under identical conditions, the $Fe_2O(bipy)_4(H_2O)_2(ClO_4)_4$/ H_2O_2 and complex **1**/TBHP systems did not display any enantioselectivity.
19. Arends, I. W. C. E.; Ingold, K. U.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1995**, *117*, 4710-4711.
20. Groves, J. T.; Van der Puy, M. *J. Am. Chem. Soc.* **1976**, *98*, 5290-5296.
21. Ménage, S.; Vincent, J.-M.; Lambeaux, C.; Fontecave, M. *J. Mol. Catal.:A* **1996**, *113*, 61-75.
22. Kaku, Y; Otsuka, M.; Ohno, M. *Chem. Lett.* **1989**, 611-614.

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