DALTON
FULL PAPER

Selective dioxygenation of cyclohexane catalysed by hydrogen peroxide and dinuclear iron(III) complexes with μ-alkoxo bridges†

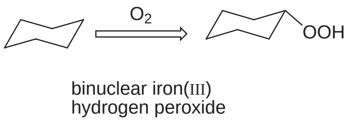
Satoshi Nishino,[a] Hiroyuki Hosomi,[b] Shigeru Ohba,[b] Hideaki Matsushima,[c] Tadashi Tokii[c] and Yuzo Nishida *[a]

[a] *Institute for Molecular Science, Myoudaijimachi, Okazaki 444-8585, Japan*
[b] *Departments of Chemistry, Faculty of Science and Technology, Keio University, Yokohama 223, Japan*
[c] *Faculty of Science and Engineering, Saga University, Saga, 841, Japan*

Received 14th December 1998, Accepted 11th March 1999

Several dinuclear iron(III) complexes with μ-alkoxo bridges gave predominantly cyclohexyl hydroperoxide in the reaction with cyclohexane and hydrogen peroxide, and similar results were observed when linear *n*-alkanes, such as *n*-nonane and *n*-octane, were used instead of cyclohexane. A mechanism for selective formation of the hydroperoxide is discussed.

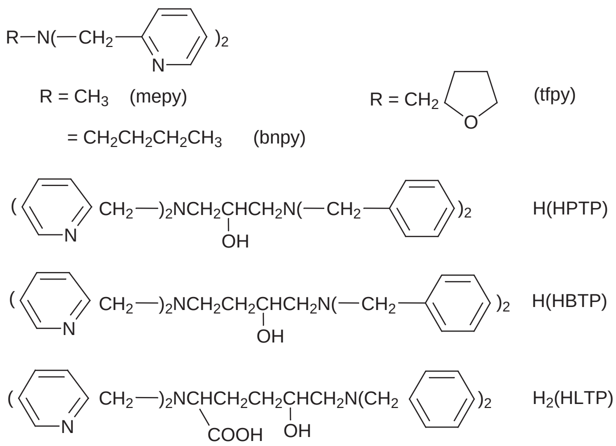
The selective oxidation and functionalization of alkanes under mild conditions is an exciting scientific and economic goal.[1] Although much of the research has focused on oxidation catalysed by metalloporphyrins (putative cytochrome P-450 mimics),[2] there is a growing interest in catalysis by other types of metal compounds. Fontecave and co-workers[3] and Fish *et al.*[4] have observed that dinuclear oxo-bridged non-heme iron complexes with pyridine or tetradentate ligands exhibit high activity for oxygenation of cyclohexane in the presence of hydrogen peroxide. They also have reported that cyclohexyl hydroperoxide forms in the reaction mixture (see below),[4] but the formation mechanism remains unclear at present. In this study we have observed that dinuclear iron(III) complexes with μ-alkoxo bridges have high activity for the selective formation of cyclohexyl hydroperoxide in the presence of hydrogen peroxide and cyclohexane, and discuss the origin for the high selectivity of the complex. Similar selective dioxygenation reactions were also observed for the linear alkanes, such as *n*-nonane and *n*-octane.



Experimental

Materials

The binuclear iron(III) compounds used are $[Fe_2O(CH_3CO_2)_2(L)_2][ClO_4]_2$,[5] $[Fe_2(HPTP)Cl_4]ClO_4$,[6] $[Fe_2(HBTP)Cl_4]ClO_4$ and $[Fe_2\{H(HLTP)\}Cl_3][PF_6]_2$ (see below), where (L) represents tridentate ligands, such as (tfpy) or (mepy). The compound $[Fe_2(HBTP)Cl_4]ClO_4$ was obtained as follows: a methanol solution (20 ml) of H(HBTP) (460 mg) was added to a methanol solution (30 ml) containing $FeCl_3\cdot 6H_2O$ (540 mg) and $NaClO_4$ (100 mg), and the deposited yellow precipitate was recrystallized from a methanol–acetonitrile (1 : 1 v/v) solution to give yellow prisms {Found: C, 39.32; H, 4.26; N, 9.54. Calc. for $[Fe_2(HBTP)Cl_4]ClO_4\cdot 2H_2O$: C, 39.26; H, 4.12; N, 9.81%}. The ligand $H_2(HLTP)$ was obtained according to the method described for the preparation of H(HPTP),[6] using 5-hydroxy-DL-lysine (Aldrich) and 2-methylpyridyl chloride. By mixing a methanol solution of $H_2(HLTP)$ and iron(III) chloride hexahydrate, a yellow precipitate was obtained {Found: C, 37.58; H, 4.15; N, 8.91. Calc. for $[Fe_2(HLTP)Cl_3][FeCl_4]\cdot 0.5H_2O$: C, 37.92; H, 3.71; N, 8.84%}. By recrystallizing the yellow compounds from an acetonitrile–methanol solution containing NH_4PF_6 the corresponding PF_6 salt was obtained {Found: C, 35.30; H, 3.56; N, 8.53. Calc. for $[Fe_2\{H(HLTP)\}Cl_3][PF_6]_2$: C, 34.90; H, 3.22; N, 8.14%}. The formation of the dinuclear $[Fe_2(HLTP)Cl_3]PF_6$ species was confirmed in the solution by Electrospray Mass Spectrometry (ESI-MS) (see Fig. 3).



Crystal structure determination

The crystal structures of the green $[Fe_2O(CH_3CO_2)_2(mepy)_2][ClO_4]_2\cdot H_2O$ **1** and red $[Fe_2O(CH_3CO_2)_2(bnpy)_2][ClO_4]_2$ **2** complexes were determined (see Table 1).

CCDC reference number 186/1384.

Reaction of iron(III) compounds with cyclohexane in the presence of hydrogen peroxide

In a typical run, hydrogen peroxide [0.01 mol; acetonitrile solution (10 cm^3) containing 1.13 g of 30% commercial hydrogen peroxide solution] was added dropwise (within 5 min) to an

---

† *Supplementary data available*: ORTEP drawing of $[Fe_2(HPTP)Cl_4]^+$, plots of turnover number, AM1 calculations, gas chromatogram. Available from BLDSC (No. SUP 57518, 32 pp.). See Instructions for Authors, 1999, Issue 1 (http://www.rsc.org/dalton).

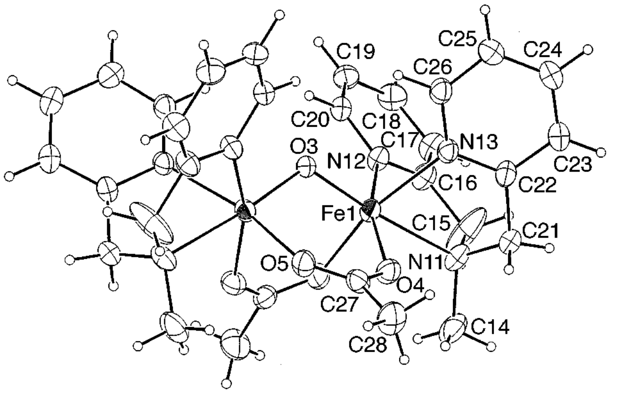


Fig. 1 An ORTEP drawing of $[Fe_2O(CH_3CO_2)_2(mepy)_2]^{2+}$ (50% probability).

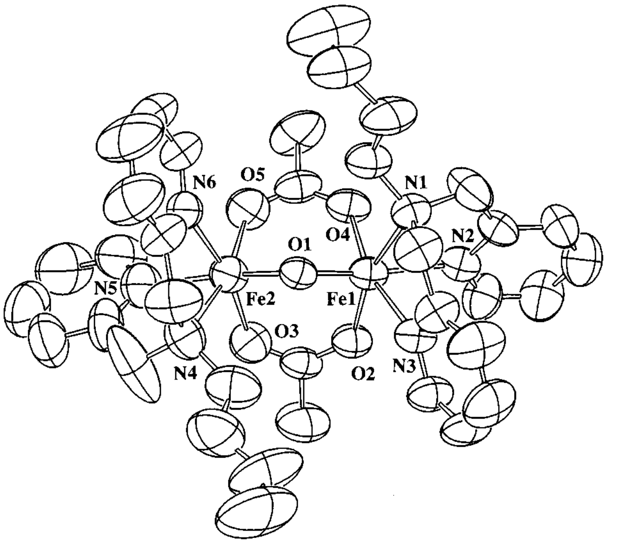


Fig. 2 An ORTEP drawing of $[Fe_2O(CH_3CO_2)_2(bnpy)_2]^{2+}$ (50% probability).

acetonitrile solution (30 cm^3) containing iron(III) complex (0.01 mmol) and cyclohexane (0.01 mol), and the products were determined by GC after the usual work-up. Turnover number is [mole of product]/[mole of iron(III) complex used]. An authentic sample of cyclohexyl hydroperoxide was obtained according to the method of Fish *et al.*[4] and iodometric titration[4] was used to determine it. In the similar way, *n*-nonane (1 mmol, one-tenth of the case with cyclohexane) was treated with iron(III) compound and hydrogen peroxide. Authentic samples of 1- and 2-hydroperoxide derivatives of *n*-nonane and *n*-octane were obtained according to the published method.[7]

Results and discussion

Structure of the compounds

In Figs. 1 and 2 ORTEP[8] drawings of the compounds with (mepy) and (bnpy) are illustrated. The structures of these compounds are of a dimeric core with one oxo and two acetate bridges (see also Tables 2 and 3), essentially the same as those published.[9] The green (mepy) complex **1** has a crystallographic twofold axis running through the O3 atom, and two amine nitrogen atoms are co-ordinated to the position *trans* to the oxo-oxygen atom. To the contrary, two pyridine nitrogen atoms are co-ordinated to the positions *trans* to the oxo oxygen atom in the case of the red (bnpy) complex.[5]

Table 1 Crystal data of compounds **1** and **2**

	1	**2**
Formula	$Fe_2Cl_2O_{14}N_6C_{30}H_{38}$	$Fe_2Cl_2O_{13}N_6C_{36}H_{48}$
M	889.26	955.41
Crystal symmetry	Monoclinic	Monoclinic
Space group	$C2/c$	$P2_1/c$
a/Å	16.084(3)	12.408(4)
b/Å	14.704(2)	21.171(10)
c/Å	18.473(2)	17.643(6)
β/°	115.88(1)	106.67(3)
V/Å^3	3930.7(11)	4461(3)
Z	4	4
T/K	297	296
D_c/g cm^{-3}	1.503	1.428
μ(Mo-Kα)/cm^{-1}	9.44	8.36
Observed reflections	2989	2679
Variables	245	541
R	0.071	0.058
R'	0.080	0.063
Goodness of fit	1.90	1.92

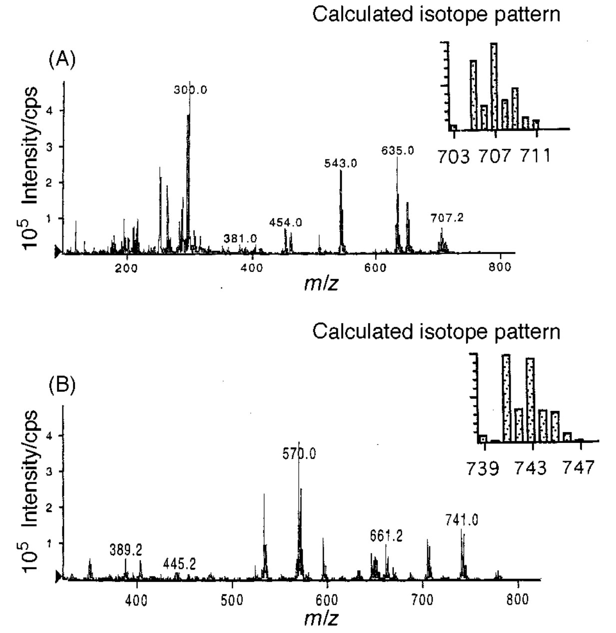


Fig. 3 ESI Mass spectra (positive pattern) and calculated isotope patterns of solutions of (A) $[Fe_2(HPTP)Cl_4]ClO_4$ and (B) $[Fe_2\{H(HLTP)\}Cl_3][PF_6]_2$.

In Fig. 3, ESI mass spectra of the iron(III) compounds $[Fe_2(HPTP)Cl_4]ClO_4$ and $[Fe_2\{H(HLTP)\}Cl_3][PF_6]_2$ are illustrated. In the dilute acetonitrile solution containing $[Fe_2(HPTP)Cl_4]^+$, whose crystal structure was determined previously,[6] several peaks are observed; a peak at m/z = 707.2 corresponds to $[Fe^{III}_2(HPTP)Cl_4]^+$, which is consistent with the calculated isotope pattern in the figure. The peaks at m/z = 635.5 may correspond to $[Fe^{II}_2(HPTP)Cl_2]^+$ species. In the case of $[Fe_2\{H(HLTP)\}Cl_3][PF_6]_2$, the peak at m/z = 741.0 should correspond to $[Fe^{III}_2(HLTP)Cl_3]^+$, indicating dissociation of a proton of the carboxylic acid of H(HLTP) occurs in solution. Anyway, the formation of an alkoxo-bridged dinuclear iron(III) species with (HLTP) ligand was confirmed.

Products from the reaction mixture containing cyclohexane

The time course of the product formation is illustrated in Figs. 4 and 5. The results for the Fe(bnpy) complex are essentially the same as those of the (tfpy) complex. All the iron(III) compounds with oxo-bridges used exhibited activity for formation of cyclohexanol, cyclohexanone and cyclohexyl hydroperoxide (see Fig. 4), which is consistent with the results reported by Fish *et al.*[4] It should be noted that the dinuclear iron(III) compounds with a μ-alkoxo bridge, for example, $[Fe_2(HPTP)Cl_4]^+$ or $[Fe_2(HBTP)Cl_4]^+$, exhibit high activity for formation of the cyclohexyl hydroperoxide, whereas the activity for cyclo-

Table 2 Selected bond distances (Å) and angles (°) of compound **1** which has a crystallographic twofold axis through the O3 atom

Fe1–O3	1.794(3)	Fe1–O3$^\mathrm{i}$	1.794(3)	Fe1–O4	2.030(4)
Fe1–O5$^\mathrm{i}$	2.051(4)	Fe1–N11	2.263(5)	Fe1–N12	2.135(5)
Fe1–N13	2.130(5)	Fe1 ··· Fe1$^\mathrm{i}$	3.0864(8)		
O3–Fe1–O4	98.4(2)	O3–Fe1–O5$^\mathrm{i}$	97.9(2)	O3–Fe1–N11	175.1(2)
O3–Fe1–N12	99.0(2)	O3–Fe1–N13	99.1(2)	O3$^\mathrm{i}$–Fe1–O4	98.4(2)
O3$^\mathrm{i}$–Fe1–O5$^\mathrm{i}$	97.9(2)	O3$^\mathrm{i}$–Fe1–N11	175.1(2)	O3$^\mathrm{i}$–Fe1–N12	99.0(2)
O3$^\mathrm{i}$–Fe1–N13	99.1(2)	O4–Fe1–O5$^\mathrm{i}$	93.7(2)	O4–Fe1–N11	84.2(2)
O4–Fe1–N12	162.3(2)	O4–Fe1–N13	89.9(2)	O5$^\mathrm{i}$–Fe1–N11	86.0(2)
O5$^\mathrm{i}$–Fe1–N12	86.7(2)	O5$^\mathrm{i}$–Fe1–N13	161.9(2)	N11–Fe1–N12	78.2(2)
N11–Fe1–N13	76.7(2)	N12–Fe1–N13	84.6(2)	Fe1–O3–Fe1$^\mathrm{i}$	118.7(3)

Symmetry code: i $-x, y, \frac{3}{2} - z$.

Table 3 Selected bond lengths (Å) and angles (°) of compound **2**

Fe1–O1	1.775(6)	Fe1–O2	2.012(7)	Fe1–O4	2.022(7)
Fe1–N1	2.205(8)	Fe1–N2	2.170(9)	Fe1–N3	2.152(9)
Fe2–O1	1.774(6)	Fe2–O3	2.023(8)	Fe2–O5	2.019(8)
Fe2–N4	2.20(1)	Fe2–N5	2.14(1)	Fe2–N6	2.15(1)
Fe1 ··· Fe2	3.075(4)				
O1–Fe–O2	99.2(3)	O1–Fe1–O4	97.2(3)	O1–Fe1–N1	92.2(3)
O1–Fe1–N2	170.2(3)	O1–Fe1–N3	97.1(3)	O2–Fe1–O4	95.2(3)
O2–Fe1–N1	164.4(3)	O2–Fe1–N2	90.3(3)	O2–Fe1–N3	90.1(3)
O4–Fe1–N1	93.9(3)	O4–Fe1–N2	84.3(3)	O4–Fe1–N3	163.8(3)
N1–Fe1–N2	78.0(3)	N1–Fe1–N3	77.9(3)	N2–Fe1–N3	80.4(3)
O1–Fe2–O3	97.1(3)	O1–Fe2–O5	98.5(3)	O1–Fe2–N4	93.6(3)
O1–Fe2–N5	172.3(3)	O1–Fe2–N6	94.6(3)	O3–Fe2–O5	93.6(3)
O3–Fe2–N4	92.9(3)	O3–Fe2–N5	82.2(3)	O3–Fe2–N6	166.4(3)
O5–Fe2–N4	165.4(3)	O5–Fe2–N5	89.2(3)	O5–Fe2–N6	91.3(3)
N4–Fe2–N5	78.8(3)	N4–Fe2–N6	79.6(3)	N5–Fe2–N6	79.6(3)
Fe1–O21–Fe2	120.1(3)				

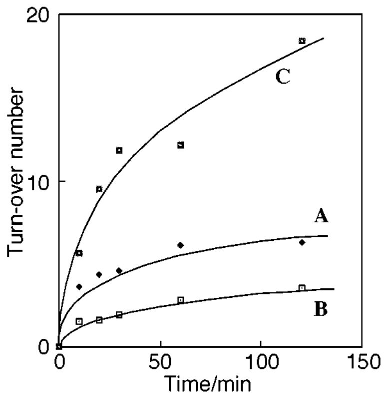


Fig. 4 Plots of turnover numbers (= [mole of product]/[mole of iron(III) complex]) of the products catalysed by red [Fe$_2$O(CH$_3$CO$_2$)$_2$(tfpy)$_2$][ClO$_4$]$_2$:[2] A, cyclohexanol; B, cyclohexanone; C, cyclohexyl hydroperoxide.

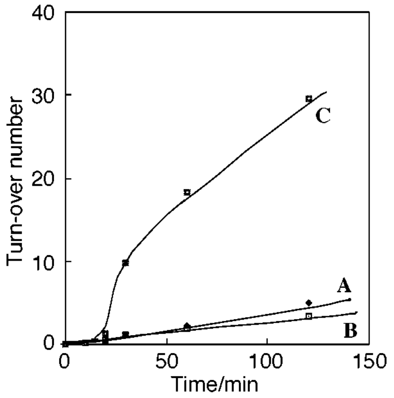


Fig. 5 Plots of turnover numbers of the products catalysed by [Fe$_2$(HBTP)Cl$_4$]ClO$_4$: A, cyclohexanol; B, cyclohexanone; C, cyclohexyl hydroperoxide.

hexanol and cyclohexanone is very low (see Fig. 5), and the activity of the (HBTP) complex for formation of cyclohexyl hydroperoxide is higher than that of the (HPTP) complex. Similar results are obtained for the linear alkane *n*-nonane (see Figs. 6 and 7), but in the cases of *n*-alkanes it was found that oxygenation reactions do not occur at the terminal carbon atoms, *e.g.* the yields of the 1-hydroperoxide of *n*-nonane, 1-hydroxy-*n*-nonane, and *n*-nonanal are negligible. In our GC experiments, we cannot distinguish the products at the 4 and 5 positions of *n*-nonane (see SUP 57518).

Mechanism of cyclohexyl hydroperoxide formation

Fish *et al.*[4] have proposed that some dinuclear iron(III) complexes with oxo-bridges, similar to those of (mepy) and (tfpy) used in this study, functionalize hydrocarbons through a well known free-radical chain process initially to generate an alkyl radical (see below). This radical is assumed to be trapped by

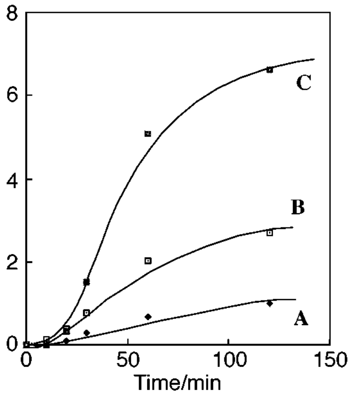


Fig. 6 Plots of turnover numbers of the products catalysed by [Fe$_2$(HPTP)Cl$_4$]ClO$_4$: A, nonan-2-ol; B, nonan-2-one; C, nonan-2-yl hydroperoxide.

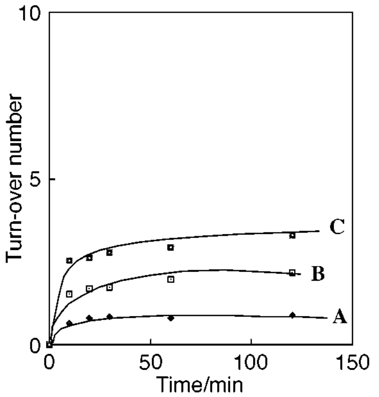
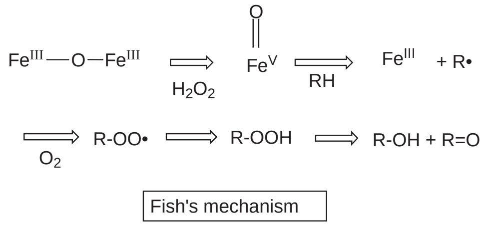
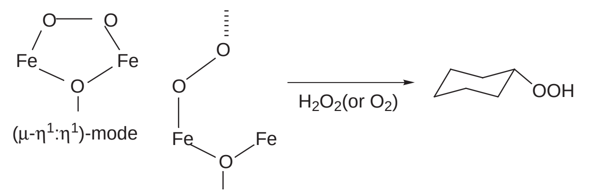


Fig. 7 Plots of turnover numbers of the products catalysed by $[Fe_2O(CH_3CO_2)_2(mepy)_2][ClO_4]_2$: A, nonan-2-ol; B, nonan-2-one; C, nonan-2-yl hydroperoxide.

oxygen to give a peroxy radical, which abstracts hydrogen from the hydrocarbon, or other hydrogen sources, to give alkyl hydroperoxide and perpetuate the chain. They believe that likely candidates for the radical initiation process include Fe–OO$^{\bullet}$ or Fe=O species, which could abstract a hydrogen atom to generate the alkyl radical (see below). However, the present results are *clearly inconsistent* with this, because the dinuclear iron(III) compounds with μ-alkoxo bridges give predominantly cyclohexyl hydroperoxide, and the yields of the corresponding alcohol and ketone are quite different from each other, especially in the cases of long linear alkanes (see Figs. 4, 6 and 7). These undoubtedly demonstrate that the structures of the active species giving cyclohexanol and cyclohexyl hydroperoxide are different from each other.



We have reported that a blue colouration occurs in solutions containing dinuclear iron(III) compounds with H(HPTP) (see Fig. 8) and H(HBTP) due to a peroxide adduct formation in the $(\mu\text{-}\eta^1:\eta^1)$ co-ordination mode (see **A** in Scheme 1).[6,10,11] In this study we have observed that (1) the blue colouration disappeared within 20 min, (2) formation of the cyclohexyl hydroperoxide is nearly zero when the dinuclear complex $[Fe_2O(CH_3CO_2)(tpa)_2]^{3+}$ is used, the latter complex being assumed to form a peroxide adduct with $(\mu\text{-}\eta^1:\eta^1)$ co-ordination mode,[12] (3) the activity of the mononuclear compound $[Fe(tpa)Cl_2]ClO_4$ to generate the corresponding hydroperoxide is much lower than those of the dinuclear compounds with μ-alkoxo bridges (see SUP 57518), where (tpa) = tris(2-pyridylmethyl)amine. These results demonstrate that the active species for the dioxygenation reaction is not a peroxide adduct with $(\mu\text{-}\eta^1:\eta^1)$-co-ordination mode (see **A** in Scheme 1), which is consistent with the presence of an induction time in the formation of cyclohexyl hydroperoxide catalysed by the Fe^{III}(HPTP) complex (see Figs. 5 and 6).



Scheme 1

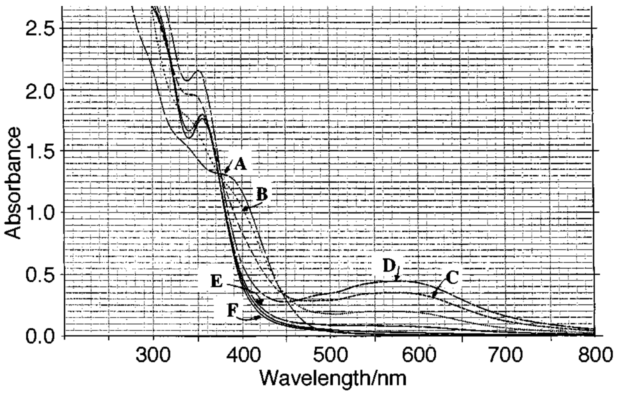


Fig. 8 Spectral changes of a solution containing $[Fe_2(HPTP)Cl_4]ClO_4$ and hydrogen peroxide {at 298 K in acetonitrile; [iron(III) complex]/$[H_2O_2]$ = 10}: A, without hydrogen peroxide; B, 0 min; C, after 5 min; D, after 10 min; E, after 60 min; F, after 120 min.

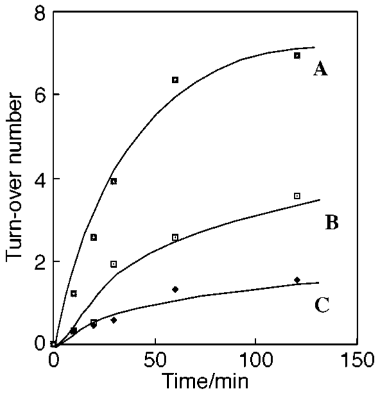
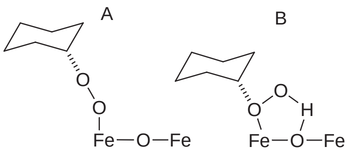


Fig. 9 Plots of turnover numbers of the products catalysed by $[Fe_2\{H(HLTP)\}Cl_3][PF_6]_2$: A, nonan-2-yl hydroperoxide; B, nonan-2-one; C, nonan-2-ol.

As shown in Fig. 8, a yellow solution forms after disappearance of the blue species (within 20 min as described above), and this yellow species should be an active species for formation of the hydroperoxide, although we have no structural information on it at present. Since it is established that the iron(III) peroxide adduct with η^1 co-ordination mode exhibits an electrophilic nature,[13–15] we would like to propose that cyclohexyl hydroperoxide is generated in solution *via* the formation of intermediate **B** in Scheme 1 through oxidative coupling (2-electron oxidation) between cyclohexane and hydroperoxide ion; in **B** the dashed line between the oxygen atom and carbon atom of cyclohexane denotes the presence of electronic interaction between them,[13–16] and in this case the approach of cyclohexane may not induce heterolytic cleavage of the O–O bond because of the lower energy of the HOMO of cyclohexane.

This is consistent with the high activity of the yellow (HLTP) complex for formation of the hydroperoxide (see Fig. 9); in this case a blue colouration does not occur upon the addition of hydrogen peroxide, which should be due to the remarkable difference in the co-ordination environments between the two iron(III) atoms. This may also explain the higher activity of the (HBTP) complex than that of the (HPTP) complex; in the former the difference in the co-ordination sites between the two iron(III) ions is larger than that in the latter.

In the cases of dinuclear iron(III) compounds with oxo-bridges, we have reported that a linear iron(III) species forms in solutions containing hydrogen peroxide.[5] In this circumstance, two types of approach by the substrate are possible as shown in Scheme 2; **A** is essentially the same as **B** in Scheme 1 for



Scheme 2

the dinuclear compounds with μ-alkoxide. In the case of **B** in Scheme 2, where formation of the hydrogen-bonded peroxide adduct has been confirmed in oxyhemerythrin[17] and the dashed line between the oxygen atom and carbon atom of cyclohexane denotes the presence of electronic interaction,[13–16] the direct hydroxylation of cyclohexane will occur through concerted heterolytic cleavage of O–O bond,[13,14] and this situation should be impossible for a bent dinuclear compound with a μ-alkoxide bridge because of steric hindrance. Thus, formation of three products catalysed by (μ-oxo)diiron(III) compounds observed in this study is elucidated by Scheme 2.

Hydroperoxide formation of linear *n*-alkanes

The HOMO and LUMO of *n*-octane based on MOPAC(AM1) calculations[18] are depicted in Fig. 10; the electronic property of *n*-nonane is essentially the same as that of *n*-octane. It should be noted that the HOMO contains no contribution from both terminal carbon atoms. Since the yields of the oxygenated products at the terminal carbon atoms are much smaller than those at other carbon atoms, for example, C-2 or C-3, it seems quite likely that the HOMO of *n*-alkane approaches the peroxide adduct through electronic interaction between the peroxide adduct and carbon atom[13–15] as shown below, and this interaction controls the yields of the products. The present results should give valuable information to elucidate the reaction mechanism of alkane dioxygenases observed by Kato and co-workers.[19]

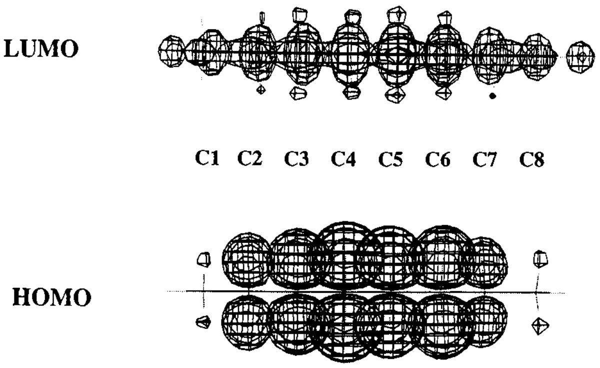
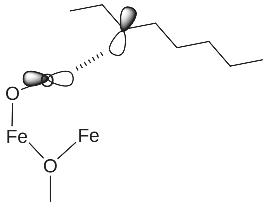


Fig. 10 Schematic illustration of the HOMO and LUMO of *n*-octane.



References

1 A. L. Feig and S. J. Lippard, *Chem. Rev.*, 1994, **94**, 759.
2 For example, M. Newcome, M.-H. T.-Biadatti, D. L. Chestney, E. S. Roberts and P. F. Hollenberg, *J. Am. Chem. Soc.*, 1995, **117**, 12085.
3 S. Menage, J. M. Vincent, C. Lambeaux and M. Fontecave, *J. Chem. Soc., Dalton Trans.*, 1994, 2081.
4 R. H. Fish, M. S. Konings, K. J. Oberhausen, R. H. Fong, W. M. Yu, G. Christou, J. B. Vincent, D. K. Coggin and R. M. Buchanan, *Inorg. Chem.*, 1991, **30**, 3002.
5 S. Ito, T. Okuno, H. Matsushima, T. Tokii and Y. Nishida, *J. Chem. Soc., Dalton Trans.*, 1996, 4037.
6 Y. Nishida, M. Nasu and T. Akamatsu, *Z. Naturforsch., Teil B*, 1992, **47**, 215.
7 H. M. Williams and H. S. Mosher, *J. Am. Chem. Soc.*, 1954, **76**, 2984, 2987.
8 C. K. Johnson, ORTEP, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, TN, 1976.
9 L. Que, Jr. and A. E. True, *Prog. Inorg. Chem.*, 1990, **38**, 97.
10 Y. Nishida and M. Takeuchi, *Z. Naturforsch., Teil B*, 1987, **42**, 52.
11 Y. Dong, S. V. Yan, V. G. Young, Jr. and L. Que, Jr., *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 618.
12 T. Okuno, S. Ito, S. Ohba and Y. Nishida, *J. Chem. Soc., Dalton Trans.*, 1997, 3547.
13 Y. Nishida, S. Ito, T. Okuno and S. Ohba, *Z. Naturforsch., Teil C*, 1997, **52**, 615.
14 S. Ito, T. Okuno, H. Itoh, S. Ohba, H. Matsushima, T. Tokii and Y. Nishida, *Z. Naturforsch., Teil B*, 1997, **52**, 719.
15 P. R. O. Montellano, *Acc. Chem. Res.*, 1998, **31**, 543.
16 K. Yoshizawa, T. Ohta, T. Shiota and T. Yamabe, *Chem. Eur. J.*, 1997, **3**, 1160; K. Yoshizawa, Y. Shiota and T. Yamabe, *J. Am. Chem. Soc.*, 1998, **120**, 564.
17 R. C. Reem, J. M. McCormick, D. E. Richardson, F. J. Devlin, P. J. Stephens, R. L. Musselman and E. I. Solomon, *J. Am. Chem. Soc.*, 1989, **111**, 4688.
18 M. J. S. Dewar, *J. Am. Chem. Soc.*, 1985, **107**, 3902.
19 J. H. Maeng, Y. Sakai, Y. Tani and N. Kato, *J. Bacteriol.*, 1996, **178**, 3695.

Paper 8/09725I