DALTON COMMUNICATION

Formation and reactivity of a peroxide adduct of iron(III) complexes containing substituted phenol derivatives

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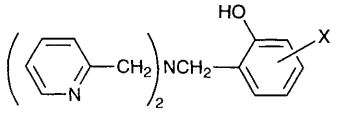
Binding of the oxygen atom of iron(III)–peroxide adducts to phenol rings has been found to be highly controlled by the substituents on the ring, implying that the interaction between the adduct and the ring involves an electronic attractive force, whereby the adduct acts as an electrophile.

Peroxoiron(III) complexes are increasingly being considered as potential intermediates in oxidations catalysed by both non-haem[1-4] and haem iron centres.[5-7] For example, electrospray mass spectrometry studies have revealed that an 'activated bleomycin' is an iron(III) peroxide complex.[8] However, evidence for the formation of iron(III)–peroxide adducts is scarce[9] and their reactivities are controversial.[10] In this study we have observed that the attack of an iron(III)–peroxide adduct on a phenol ring is greatly controlled by the substituents on the ring, implying that interaction between the adduct and the ring involves an electronic attractive force, whereby the adduct acts as an electrophile. We also have found that the iron(III)–phenol–peroxide adduct thus formed exhibits high activity for oxygenation of cyclohexane and also degradation of DNA.

The chemical structures of the phenolic compounds HL used are as illustrated; several iron(III) compounds with general formula $[FeLCl_2]$ were prepared in this study. Fig. 1 shows the crystal structures of the X = H and X = NO_2-5 compounds.*[11] In both the iron(III) has a distorted-octahedral co-ordination involving two pyridine nitrogen, an amine nitrogen, a phenolic oxygen atom and two chloride ions.



X = OMe-3, H, Br_2-3,5, NO_2-3 or -5

In the absorption spectrum (acetonitrile–water mixture) of the X = OMe-3 complex, a strong band is observed in the range 550–700 nm ($\varepsilon \approx 1300$ dm^3 mol^{-1} cm^{-1}), which has been assigned to charge-transfer transition between the phenolic moiety and iron(III).[13] When hydrogen peroxide is added the absorbance decreases and the violet solution becomes light yellow. The disappearance of the visible absorption bands is attributed to the absence of a phenolic group. This may be due

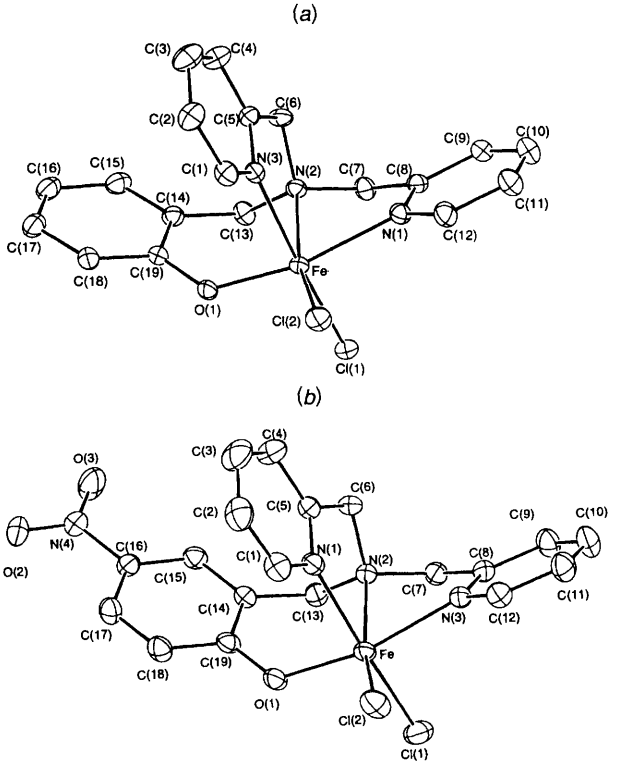
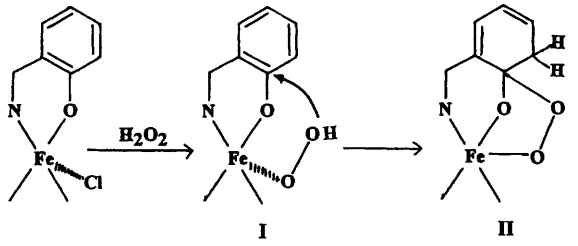


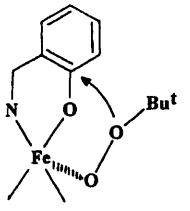
Fig. 1 The ORTEP[12] views of $[FeLCl_2]$: (*a*) X = H, Fe–Cl(1) 2.334(3), Fe–Cl(2) 2.306(3), Fe–O(1) 1.884(5), Fe–N(1) 2.217(7), Fe–N(2) 2.231(6) and Fe–N(3) 2.217(6); (*b*) X = NO_2-5, Fe–Cl(1) 2.319(1), Fe–Cl(2) 2.282(1), Fe–O(1) 1.923(2), Fe–N(1) 2.207(2), Fe–N(2) 2.232(2) and Fe–N(3) 2.193(2) Å

* The iron(III) compounds were prepared according to ref. 11: X = H [Found (calc.): C, 53.00 (52.95); H, 4.25 (4.20); N, 9.65 (9.75%)], X = OMe-3 [Found (calc.): C, 51.75 (52.10); H, 4.55 (4.35); N, 9.00 (9.10%)], X = Br_2-3,5 [Found (calc.): C, 38.75 (38.75); H, 2.90 (2.75); N, 7.15 (7.15%)] and X = NO_2-3·0.5H_2O [Found (calc.): C, 47.15 (47.05); H, 3.55 (3.75); N, 11.55 (11.55%)].

Crystal data: $[FeLCl_2]$·0.5H_2O, X = H, monoclinic, space group $P2_1/c$, a = 10.103(2), b = 7.064(2), c = 27.920(2) Å, β = 94.80(1)°, U = 1985.7(7) Å^3, Z = 4, D_c = 1.45 Mg m^{-3}, crystal dimensions 0.15 × 0.15 × 0.75 mm, R = 0.083 for 3275 observed reflections with $|F_o| > 3\sigma(|F_o|)$; $[FeLCl_2]$·MeCN, X = NO_2-5, triclinic, space group $P\bar{1}$, a = 11.944(2), b = 13.736(1), c = 7.029(1) Å, α = 98.72(1), β = 100.65(1), γ = 88.85(1)°, U = 1120.1(3) Å^3, Z = 2, D_c = 1.41 Mg m^{-3}, crystal dimensions 0.15 × 0.3 × 0.45 mm, R = 0.048 for 3778 observed reflections with $|F_o| > 3\sigma(|F_o|)$. All crystallographic measurements were made on a Rigaku AFC-5 diffractometer using Mo-Kα radiation (λ = 0.710 73 Å) at 298(2) K. Both structures were solved using direct methods for Fe, Fourier synthesis for other non-hydrogen atoms and difference synthesis for H atoms [CRYSTAN-GM Software (MAC Science) on a SUN SPARC2 workstation at Keio University] and were refined by full-matrix least squares (H atoms not included). Corrections for Lorentz and polarization effects were employed. Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 186/110.



Scheme 1



to the formation of an adduct **II** *via* adduct **I**, in Scheme 1, as exemplified for iridium(III).[14]

The absorbance decay in the visible region upon addition of H_2O_2 is highly dependent on the substituent in the phenol ring, X, decreasing in the order 3-OMe > 3-H > 3,5-Br_2 ≫ 3-NO_2, 5-NO_2. Since the complexes with X = H and NO_2-5 have the same structural features, it seems reasonable to consider that the substituent on the phenol ring may control the reactivity of adduct **I**, and consequently the formation of adduct **II**. An MNDO (modified neglect of diatomic overlap)/AM1 calculation[15] on *o*-(dimethylaminomethyl)phenol revealed that the energies of both the highest occupied and lowest unoccupied molecular orbitals (consisting of mainly π orbitals of the phenol ring) are highest and lowest for X = H and NO_2-5, respectively, among the compounds HL. This may lead to the conclusion that the main interaction between adduct **I** and the π electrons of the phenol ring involves an electronic attractive force, and the observed rate of decolouration can be reasonably explained only if we assume that **I** acts as an electrophile.[16] We also have observed that decolouration of the iron(III) complexes occurs on addition of *tert*-butyl hydroperoxide, the rate being the same as that for the hydrogen peroxide system. This indicates that the Bu^tO_2H adduct also acts as an electrophile, and this supports our conclusion that adduct **II** in Scheme 1 is electrophilic.

In order to get more information on adduct **II**, we have studied the formation of oxygenated products in the reaction with a saturated alkane such as cyclohexane.* Table 1 shows that the complexes with X = H or OMe-3 are highly active for the formation of oxygenated cyclohexane, but the activity when X = NO_2-5 is almost negligible. Since the decolouration does not occur in the latter solutions containing H_2O_2, it is clear that adduct **II** is an intrinsic species for oxygenation of cyclohexane. Its electrophilic nature may be the main reason why the complex with X = H can oxygenate cyclohexane in the presence of H_2O_2. To elucidate the reactivity of adduct **II**, we have investigated the degradation of DNA by this system.† The X = H complex exhibits high activity towards relaxation of pBR322 Form I DNA (supercoiled) to Form II (relaxed circular) and also to Form III (linear duplex)[18] under experimental conditions where free iron(III) ion cannot effect such relaxation. This activity is very similar to that of bleomycin,[19] and thus the present results should give useful information for elucidating the reaction mechanism of DNA degradation by the iron(III)–bleomycin–H_2O_2 system.[20]

Table 1 Turnover numbers (mol of product/mol of iron(III) complex used) of the oxygenation products

X	Cyclohexanol	Cyclohexanone
H	2.8	2.4
OMe-3	2.6	2.4
NO_2-5	0.0	0.0
*	0.4	0.1

* $[Fe\{N(CH_2C_5H_4N\text{-}2)_3\}Cl_2]ClO_4$.[17]

* Typically, an acetonitrile solution (20 cm^3) containing iron(III) complex (0.05 mmol) and cyclohexane (840 mg) was added to an acetonitrile solution (10 cm^3) containing H_2O_2 (1.13 g of 30% aqueous solution), and after 3 h the oxygenated products were determined by GC. Cyclopentanone was used as an internal standard.

† DNA (supercoiled pBR322) was obtained from Wako Chemicals. Typically, an iron(III) complex (4 μl of 0.1 mmol dm^{-3} solution), DNA (4 μl of 0.1 μg per μl solution), tris(hydroxymethyl)aminomethane buffer (3 μl of 0.1 mol dm^{-3} solution) and H_2O_2 (4 μl of 10 mmol dm^{-3} solution) were mixed and allowed to stand for 1 h at 25 °C. The extent of DNA cleavage was assessed by analysis on 0.9% agarose gel containing ethidium (3,8-diamino-5-ethyl-6-phenylphenanthridium) bromide.[18] The bands were photographed with Polaroid 667 film.

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