Direct Observation of Push Effect on the Heterolytic O–O Bond Cleavage Reaction of Acylperoxo-Iron(III) Porphyrin Adducts

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We report the first direct observation of the push effect of the sixth ligand on the heterolytic O–O bond cleavage step of acylperoxo-iron(III) porphyrin complexes to the corresponding oxo-ferryl porphyrin π-cation radicals by utilizing a series of imidazole derivatives.

The elucidation of the O–O bond cleavage process of hydroperoxo-iron(III) porphyrin complexes yielding active high-valent oxo species is very important to understand the nature of the oxygen activation mechanisms by haem enzymes such as cytochrome P-450, peroxidases and catalase.[1] It has been proposed that the proximal ligands of these haem enzymes such as thiolate, imidazolate and phenolate serve as strong internal electron donors to destabilize the O–O bond of hydroperoxo-iron(III) porphyrin (*push effect*),[2] and distal base residues are considered to favour the heterolytic O–O bond cleavage (*pull effect*).[3] The push–pull mechanism has been examined by using synthetic haem model systems.[4–6] On the other hand, we have reported that the reaction of perbenzoic acid and Fe^{III} porphyrins bearing a hydroxo ligand **1** [Fe(OH)] in dry CH_2Cl_2 at low temperature gives peracid-Fe^{III} adducts as an irreversible process followed by a heterolytic cleavage of the O–O bond of the adducts to form the corresponding oxo-ferryl porphyrin cation radicals (Scheme 1).[6a–c,g,7] These stepwise reactions are directly observable by employing low-temperature UV–VIS measurement. Thus, the rate constants (k_{dec}) of the O–O bond cleavage of five coordinated acylperoxo-Fe^{III} porphyrins **2** in CH_2Cl_2 at low temperature have been reported.[6c,g]

Here, we have examined the stoichiometric reaction of imidazole derivatives and **5** in a CH_2Cl_2 solution at low temperature in order to understand the push effect of the sixth ligand and found the immediate formation of peracid-Fe^{III}-imidazole ternary complexes **4** followed by the heterolytic O–O bond cleavage of **4** to yield oxo-ferryl porphyrin π-cation radicals.

The push effect of the sixth ligand on the heterolysis of the O–O bond: In a typical reaction, a methylene chloride solution of hydroxo-iron(III) TDMPP[8] (**1**; 2.0×10^{-5} mol dm^{-3}) was cooled to −80 °C in a UV–VIS cuvette. Introduction of 1.2 equiv. of *m*-chloroperbenzoic acid (MCPBA) to the solution immediately produced acylperoxo-iron(III) porphyrin **2** followed by isosbestic spectral changes affording an oxo-ferryl porphyrin cation radical **3** according to heterolytic O–O bond cleavage as reported before (Fig. 1, inset).[6c,g,9] In contrast, addition of 1 equiv. of 1-phenylimidazole (1-Ph-Im) after the formation of **2** was found to give a new intermediate which exhibits a UV–VIS spectrum typical of six coordinated ferric low-spin complex (**4** in Fig. 1).[9]

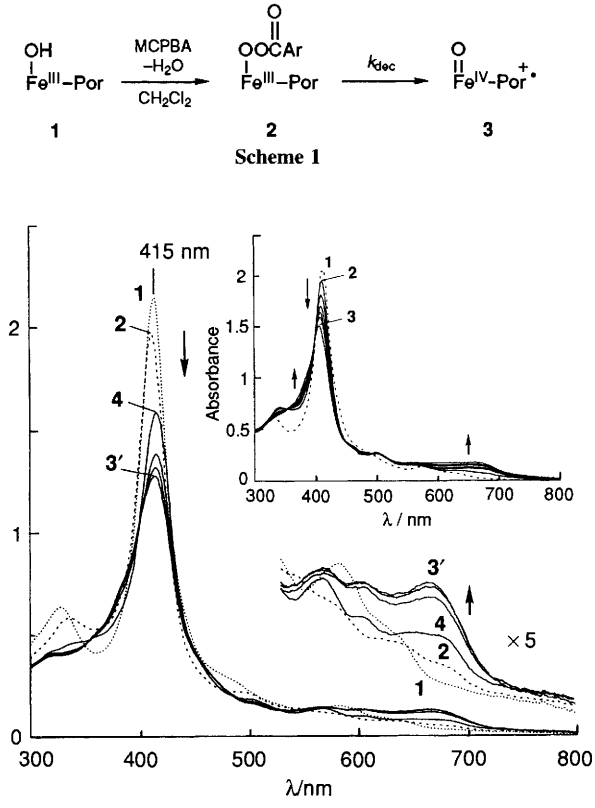


Fig. 1 Effect of 1-phenylimidazole (1 equiv.) on the reaction of 2.4×10^{-5} mol dm^{-3} of hydroxoiron(III) porphyrin (**1**: ···) and 1.2 equiv. of MCPBA in methylene chloride at −80 °C. The spectrum of **2** (- - -) was recorded immediately after the addition of MCPBA. The spectrum of **4** (——) was recorded immediately after the addition of 1-phenylimidazole. The transformation of **4** was recorded every 5 min. Inset: time dependent spectral changes in the reaction of Fe^{III}TDMPP(OH) and MCPBA in methylene chloride at −80 °C.

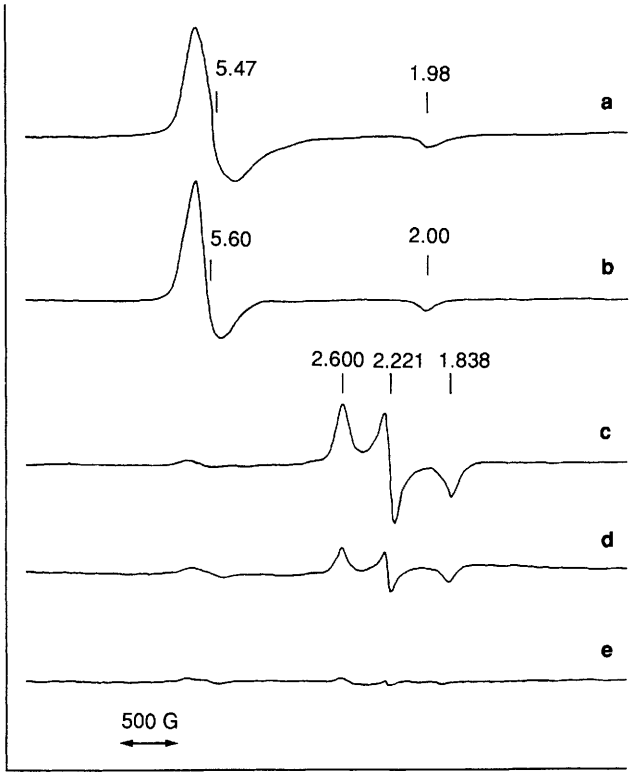
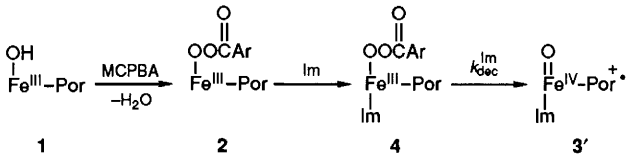


Fig. 2 Time-dependent EPR spectral changes in the stoichiometric reaction of **1** and MCPBA (8.0×10^{-3} mol dm^{-3}) in methylene chloride at −78 °C. Each sample was frozen (77 K) for measurement, **a**: a methylene chloride solution of **1**, **b**: sample immediately after the addition of MCPBA to the solution of **a**, **c**: sample immediately after the introduction of 1 equiv. of 1-phenylimidazole to the solution of **b**, **d** and **e**: time-dependent EPR spectral changes of **c**.



Scheme 2

Table 1 Effect of the sixth ligand on the first-order rate constants for the O–O bond cleavage of **2** and **4**

Imidazole	$k^{(Im)}_{hetero}$[a]/$10^{-3}s^{-1}$
Without Im	0.3 ± 0.2
1-Me-5-Cl-Im	0.6 ± 0.2
1-Ph-Im	2.0 ± 0.1
I-Me-Im	16.6 ± 0.6

[a] 1.2 equiv. of *m*-chloroperbenzoic acid was used in CH_2Cl_2 at −80 °C.

Table 2. Temperature dependence of the first-order rate constants for the O–O bond cleavage of acylperoxo-Fe^{III}TDMPP and acylperoxo-Fe^{III}TDMPP(1-Ph-Im)

	$k^{(Im)}_{hetero}$[a]/$10^{-3}s^{-1}$	
T/°C	Without Im	1-Ph-Im
−40	3.9 ± 0.2	11.2 ± 0.5
−50	2.4 ± 0.1	8.4 ± 0.4
−60	1.3 ± 0.1	5.5 ± 0.2
−70	0.6 ± 0.2	3.4 ± 0.1
−80	0.3 ± 0.2	2.0 ± 0.1
−90	*b*	1.2 ± 0.1

[a] 1.2 equiv. of *m*-chloroperbenzoic acid was used in CH_2Cl_2. [b] Not available.

Further, conversion of **4** into the oxo-ferryl cation radical **3′** is evident from isosbestic changes of UV–VIS spectra. On the basis of stoichiometric formation, spectral features and reactivity of **4**, the structure of **4** is assigned to be a six coordinated low-spin acylperoxo-Fe^{III}TDMPP(1-Ph-Im). Further evidence for the stoichiometric formation of the acylperoxo-iron(III)-imidazole adduct was obtained from the electron paramagnetic resonance (EPR) spectrum of Fe^{III}TDMPP(MCPBA)-(1-PhIm) at 77 K. Upon the introduction of MCPBA at −78 °C, a small EPR spectral change due to the replacement of the fifth ligand was observed (Fig. 2, **a** → **b**). Addition of 1-Ph-Im to the resulting solution gave a EPR spectrum characteristic of six coordinated ferric low-spin complexes (**b** → **c**).[10] Finally, EPR signals disappeared according to the formation of **3′** [(**c** → **d** → **e**)].[11] Replacement of 1-Ph-Im by either 1-methyl-5-chloroimidazole or 1-methylimidazole in the reaction with **2** also afforded **3′** *via* instantaneous formation of six coordinated low spin intermediate **4**.

On the basis of the UV–VIS spectral changes shown in Fig. 1, the O–O bond cleavage of **4** was found to be first order in [**4**], consistent with the reaction mechanism shown in Scheme 2. Values of the rate constants $k^{(Im)}_{hetero}$ for the formation of **3′** in the presence and absence of a series of imidazole derivatives are summarized in Table 1. Apparently, electron-rich imidazoles accelerate the heterolytic O–O bond-cleavage step, whereas electron-poor imidazole is less effective. These observations of the push effect mediated by *N*-substituted imidazoles provide the first direct evidence to support the proposed role of strong electron donor, anionic imidazole of proximal histidine, for the formation of Compound I in the peroxidase reactions.[2] The results are consistent with the push effect of substituents at the *meso*-positions of a porphyrin ring on the heterolysis of the O–O bond.[6g]

In order to determine the activation parameters for the O–O bond cleavage, the formation of **3′** in the presence and absence of 1-Ph-Im was examined between −40 and −90 °C. Linear Arrhenius plots were obtained based on the results listed in Table 2. The activation energies for the formation of **3′** in the presence and absence of 1-Ph-Im were determined to be 3.9 and 5.9 kcal mol^{-1} (1 cal = 4.184 J), respectively. The result suggests that the coordination of a sixth ligand stabilizes the transition state in the O–O bond-cleavage reaction.

In conclusion, it has been shown that the electron-rich sixth ligands strongly enhance the heterolysis of the O–O bond of acylperoxo-iron(III) TDMPP-imidazole complexes to yield the corresponding oxo-ferryl porphyrin cation radicals.

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