Reaction of Iron(III) Porphyrin Hydroxide with Imidazoles

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The reaction of 5,10,15-trianthracenyl-20-(4-methoxyphenyl)porphyrinato iron(III) hydroxide (**2**), with imidazole or 1-methylimidazole yields a new bis-imidazole complex whose suggested structure comprises bis ligation by one imidazole and the hydroxide with the latter hydrogen-bonded to a second imidazole.

Among the many ways that the protein environment influences heme protein chemistry is steric blocking which prevents μ-peroxo dimer formation in the binding of dioxygen to $\mathrm{Fe^{II}}$ porphyrin or μ-oxo dimer formation of $\mathrm{Fe^{III}}$ porphyrins in an alkaline medium.[1] Biomimetic approaches to modelling dioxygen binding or preparing high valent analogues related to cytochrome P-450 and peroxidase intermediates have used the strategy of incorporating blocking groups *via* the phenyl rings of tetraphenylporphyrin (TPP).[2—6] In several reports,[2—7] characteristics of the compound formed by reaction of bifacially blocked $\mathrm{Fe^{III}}$ porphyrin and hydroxide have led to proposals that a hematin derivative, $\mathrm{Fe^{III}}$ porphyrin hydroxide, is formed rather than the usual μ-oxo $\mathrm{Fe^{III}}$ dimer. An *X*-ray structure of a hydroxoiron(III) α,γ-dialkyl porphodimethene has been published recently.[7]

We report here the synthesis and characterization of $\mathrm{Fe^{III}}$ porphyrin hydroxide and its reactions with imidazoles. The bifacially hindered porphyrin, 5,10,15-trianthracenyl-20-(4-methoxyphenyl)porphyrin (TAPP) was prepared by condensation of 9-anthraldehyde, anisaldehyde, and pyrrole.‡ Insertion of iron as $\mathrm{Fe^{II}}$ acetate in benzene–acetic acid (1:2) and chromatography on alumina followed by stirring with aqueous KCl afforded the iron complex as the chloride $\mathrm{Fe^{III}TAPPCl}$ (**1**). The optical spectrum of (**1**) is the usual high spin spectrum, Figure 1. When a $\mathrm{CH_2Cl_2}$ solution of (**1**) was stirred with aqueous KOH, the compound formed exhibited the optical spectrum shown in Figure 1. It is neither that of typical high-spin $\mathrm{Fe^{III}}$ complexes nor that of the antiferromagnetically coupled $\mathrm{Fe^{III}}$ μ-oxo dimer. The spectrum is remarkably similar

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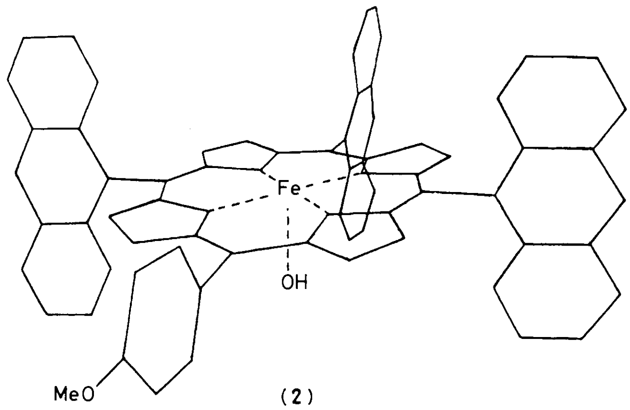
‡ *Conditions:* 9-anthraldehyde–anisaldehyde (3:1) in benzene–acetic acid (4:1). Chromatography on silica gel with hexane–benzene (1:1) affords the free base of (**1**) in 0.5% yield.

to that of the high-spin Fe^{III}TPP methoxide.[8] An identical spectrum was found by addition of tetraethylammonium hydroxide or methanolic KOH to (**1**).

Fe^{III}TAPPCl (**1**)
Fe^{III}TAPP(OH) (**2**)
Fe^{III}TAPP(Im)$_2$Cl (**3**)
Fe^{III}TAPP(Im)$_2$OH (**4**)
Fe^{III}TAPP(1-MeIm)$_2$Cl (**5**)

Characterization of the compound as the monomeric Fe^{III} porphyrin Fe^{III}TAPP(OH) (**2**) was based on chemical and physical properties.§ Titration with HCl–benzene showed that a ratio of 1:1 base:FeTAPP was present. In CCl$_4$ an i.r. absorption at 3660 cm^{-1} (ν_{OH}) shifted to 2700 cm^{-1} when NaOD was the base. The magnetic susceptiblility of (**2**) obeyed the Curie law from 220 to 320 K and was found to be 5.7 μ_B by the Evans method, a result that is consistent with high-spin (S 5/2) iron, as is the ^{1}H n.m.r. β-pyrrole signal observed at δ 79.6. These observations exclude a μ-oxo form. In dry toluene glass at 77 K, the e.s.r. spectrum of (**2**) was that of high-spin iron with three species of different e.s.r. signatures corresponding to 14, 5, and 0% rhombicity.[9] No simplification of the spectrum occurred at *ca.* 4 K. Under the same conditions (**1**) exhibited an axially symmetric e.s.r. signal. Although (**2**) is electrochemically irreversible in CH$_2$Cl$_2$ at Pt, the phenoxathiine cation radical cleanly oxidized (**2**) in a one-electron step. The oxidized porphyrin was reduced to (**2**) by addition of 1,4-diazabicyclo[2.2.2]octane (1 equiv.). The optical spectrum of the product is similar to that of oxidized FeTPPCl[10] which is thought to be a cation radical of Fe^{III}TPPCl (Figure 1).[11]



(**2**)

Double bonds have been omitted for clarity.

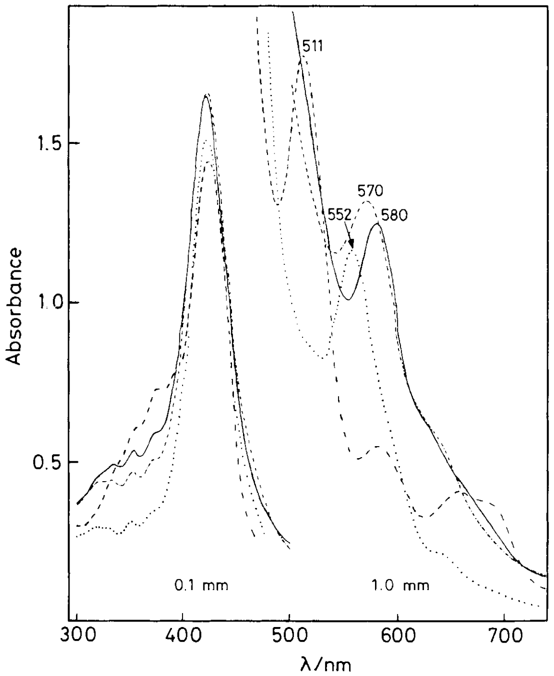


Figure 1. Optical spectra of 5,10,15-trianthracenyl-20-(4-methoxyphenyl)porphyrinatoiron(III) complexes in CH$_2$Cl$_2$. Compound (**1**) (---), (**2**) (——), (**3**) (·····), and (**4**) (–·–·). [(**1**)],[(**3**)] = 0.90 mM; [(**2**)],[(**4**)] = 0.99 mM. The optical path lengths are indicated.

Stepwise addition of imidazole (Im) to (**1**) in CH$_2$Cl$_2$ or toluene afforded only the normal bis-imidazole Fe^{III} porphyrin (**3**) whose 10 K e.s.r. spectrum is characterized by g_z 2.90 and g_x 2.33. The λ_{max} at 552 nm is the same (Figure 1) as found[12] with FeTPP(Im)$_2^+$. In CH$_2$Cl$_2$, titration of (**2**) with Im led to a new complex (λ_{max} 570 nm, Figure 1). A large excess of Im caused the change in absorption from 570 nm to the normal band at 552 nm. When the same experiment was carried out in toluene, Fe^{III}TAPP(Im)$_2$OH (**4**) was precipitated.¶ The solid exhibited a complicated low-spin e.s.r. spectrum with principal features at g 2.90 and 2.33 and additional maxima at 3.14 and 2.59, and the visible absorption spectrum, shown in Figure 1, has a maximum at 565–570 nm, rather than at 552 nm. Power saturation experiments at 4 K suggested that the feature at g 2.59 was due to a species distinct from those responsible for the remaining signals. Redissolving the solid in CH$_2$Cl$_2$ gave only a mixture of (**2**) and the 570 nm absorbing species. Distinctive behaviour was also noted when 1-MeIm was employed. Compound (**1**) or FeTPPCl formed a normal bis(1-MeIm) complex, while (**2**) led to a new complex absorbing at 535 (12.4 × 10^3 dm^3 mol^{-1} cm^{-1}) and 567 nm (10.4 × 10^3). Reactions between (**2**) and either imidazole went to completion and isosbestics were observed in the optical spectrum. In the case of (**2**) and an excess of 1-MeIm in toluene, the normal bis-imidazole, Fe^{III} porphyrin (**5**) was formed and precipitated slowly (1 h, room temperature).

Normal Fe^{III} porphyrin bis-imidazoles are formed by axial *N*-ligation of both imidazoles and by concurrent anion displacement.[13] However, the 570 nm absorbing species is also a bis-imidazole complex.[14] Since (i) different species were also found in the reaction of 1-MeIm with (**1**) and (**2**), (ii) the optical spectrum of (**4**) is dissimilar to that reported for FeTPP(Im)(Im$^-$) in that the bathochromic shift from 552 to 570 nm is far larger in the former than that observed in the latter,[15] and (iii) no evidence is found for g_z 2.7—2.8, characteristic of FeTPP(Im)(Im$^-$);[16] attack by displaced OH$^-$ on the Im hydrogen is excluded. In view of the slight optical perturbation with added Im, we suggest OH$^-$ remains as an iron ligand and participates in a hydrogen-bonding interaction with an imidazole nitrogen. The suggested structure then would comprise Fe^{III} ion bis-ligated by one imidazole and one hydroxide with the latter hydrogen bonded to the second imidazole. The structure is supported by an observed g-value at 2.59, which is close to that reported at 2.55 in Fe^{III} myoglobin hydroxide;[17] however, we cannot exclude the possibility that this feature is due to crystallinity of the sample. Evidence for the role of hydrogen bonding to an axial ligand by the distal histidine in oxygen binding heme proteins has been recently presented.[18]

The relevance of the suggested structure to heme protein

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§ Similarities of physical properties between (**1**) and other Fe^{III} porphyrin hydroxides are (i) optical, refs. 3 and 4, (ii) i.r., ref. 5, and (iii) e.s.r. spectra, ref. 4.

¶ Satisfactory elemental analyses were obtained.

chemistry may be found in the alkaline form of horseradish peroxidase.[19] Here, hydrogen bonding between a ligand at the sixth co-ordination position of iron and a distal ligand was proposed to account for acid–base catalysis by the peroxidase.[20]

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