Unusually Stable Monothiolate and S/N, S/O Mixed Ligand Complexes of Iron(III) Tetramesitylporphyrin

C. Brewer

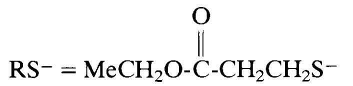
Chemistry Department, Catholic University of America, Washington, DC, 20064, U.S.A.

The reaction of tetramesitylporphinatoiron(III) hydroxide with ethyl 3-mercaptopropionate in toluene generates the air and temperature stable five co-ordinate iron(III) monothiolate complex, which adds imidazole or other Lewis base to give a six co-ordinate adduct, the unusual stability of which allows characterization by UV-VIS spectrophotometry at room temperature.

Iron(III) porphyrin monothiolate complexes have been synthesized as models of the high spin ($S = 5/2$) iron(III) state of cytochrome P450.[1—7] A major obstacle to the study of these complexes is their instability in solution toward reduction to the iron(II) state in the presence of thiolate. This problem has been overcome partially using a combination of electronegative (less reducing) thiols and porphyrin ligands which have been found to stabilize the iron(III) oxidation state. As a consequence, most iron(III) thiolate complexes have been synthesized from aryl thiolates and either octaethylporphyrin or protoporphyrin IX dimethyl ester (PPIXDME). In addition to their instability toward reduction, monothiolate complexes have also been found to be unstable in the presence of air, forming the μ-oxo dimer and disulphide upon exposure.[3,7] There is also interest in mixed adducts containing thiolate and another Lewis base, particularly imidazole (ImH), in the light of the question of the identity of the sixth axial ligand in the low spin iron(III) state of P450. Again spectral investigations of these complexes are hampered by their tendency to undergo reduction to an iron(II) species. At −50 °C and below, ESR evidence has been obtained indicating the formation of six co-ordinate low spin iron(III) complexes postulated as the mixed adduct;[3,5] and for some O donors, low temperature electronic spectra of iron(III) PPIXDME were obtained (Table 1) that are consistent with this formulation.[3] However, no optical evidence for the formation of the mixed thiolate/imidazole iron(III) porphyrin adduct has been obtained previously.

This work reports the production of a new iron(III) tetra-arylporphyrin alkylthiolate complex which is stable in air and at room temperature in toluene solution. Reaction of the monothiolate complex with several Lewis bases produces stable mixed thiolate/Lewis base adducts containing S,N and S,O donors, and their room temperature electronic spectra are reported. Most notably, the first spectra of stable mixed adducts of iron(III) porphyrins containing a thiolate and several imidazole derivatives are reported. The extraordinary stability of these complexes is attributed to the use of an electronegative alkyl thiolate, ethyl 3-mercaptopropionate, and a slightly hindered porphyrin.

$$\mathrm{FeTMPOH} + \mathrm{RSH} \rightarrow \mathrm{FeTMPSR} + \mathrm{H_2O} \qquad (1)$$



$$\mathrm{RS^-} = \mathrm{MeCH_2O\text{-}}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{\text{-}CH_2CH_2S^-}$$

When tetramesitylporphinatoiron(III) hydroxide, FeTMPOH, is reacted with excess ethyl 3-mercaptopropionate, EMP, in toluene at room temperature, a new species is observed with UV-VIS bands consistent with a normal high-spin five co-ordinate iron(III) complex as shown in Figure 1. This new complex is formulated as the monothiolate complex of FeTMP$^+$ formed by the reaction in equation (1). In the absence of air, the new complex is gradually reduced to the four co-ordinate iron(II) species, but under aerobic conditions, the iron(III) complex is stable for several hours in solution. A titration of FeTMPOH with EMP shows conversion to the thiolate species with clean isosbestic points, indicating the presence of only two porphyrin species in solution, FeTMPOH and FeTMPSR. Unlike monothiolate iron(III) porphyrins reported previously, formation of the μ-oxo dimer is not observed. This stability can be attributed to steric restrictions imposed by the mesityl groups of the porphyrin. A similar argument explains the formation of the five co-ordinate hydroxy compound rather than the μ-oxo dimer when FeTMPCl is reacted with aqueous NaOH.[8]

Toluene solutions of FeTMP(EMP) were treated with imidazole and substituted imidazoles, and the reaction products were studied by UV-VIS spectroscopy. Addition of

Table 1. UV-VIS spectral bands for FeTMP(EMP)(L).

	Wavelength/nm			
FeTMP (EMP) (ImH)[a]	430.6	543.8	623.1	
FeTMP (EMP) (4-MeImH)[a]	431.3	545.6	623.8	
FeTMP (EMP) (1,2-$\mathrm{Me_2}$Im)[a]	431.0	528.8	651.9	
FeTMP (EMP) (DMF)[b]	423.8	532.5	575.0 sh	
FeTMP (EMP) (MeOH)[c]	418.1	527.5	575.0 sh	
FeTMP (EMP) (THF)[d]	418.8	525.6	575.0 sh	
FeTMP (ImH) (Im)	418.1	553.8	590 sh	
ox P450 cam (aq)[e]	417	535	571	
Mitochrondrial ox P450 (aq)[f]	417	535	569	
Fe(PPIXDME) ($\mathrm{SC_6H_4NO_2}$) (2-MeTHF)[g,h]	418	535	566	678
Fe (PPIXDME) ($\mathrm{SC_6H_4NO_2}$) (DMF)[g,i]	420	533	567	683

[a] In toluene. [b] In DMF. [c] In methanol. [d] In THF. [e] Ref. 13. [f] Ref. 14. [g] Ref. 3. [h] In 2-methyltetrahydrofuran. [i] In toluene–methylcyclohexane.

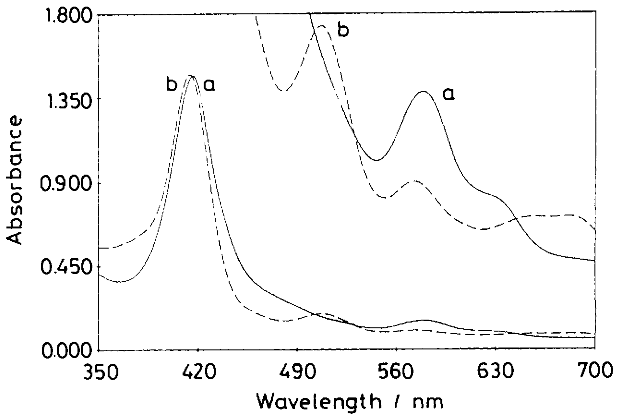


Figure 1. UV-VIS spectra of (a) FeTMPOH in toluene and (b) FeTMPOH + EMP in toluene.

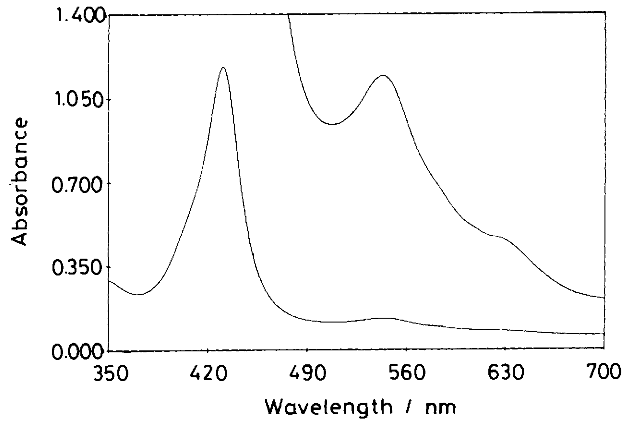


Figure 2. UV-VIS spectrum of FeTMPOH + EMP + ImH in toluene.

imidazole (Figure 2), 4-methylimidazole, and 1,2-dimethylimidazole resulted in the formation of a new species with absorptions characteristic of six co-ordinate low-spin iron(III) porphyrins. All three exhibit an unusually high wavelength Soret absorption between 430 and 432 nm and two bands in the α, β region. The UV-VIS absorptions of these complexes are given in Table 1 along with data for other complexes of interest and are attributed to the thiolate/imidazole mixed adduct of $FeTMP^+$. Unusually high wavelength Soret absorptions have been observed previously for iron(III) complexes containing two imidazolates[9] or a peroxo ligand.[10] The 430.6 nm Soret band for the complex with imidazole might therefore be expected if one axial site were occupied by a thiolate anion. The order of addition of reagents is unimportant. Addition of ImH to FeTMPOH in toluene produces FeTMP(ImH)(Im) (Table 1), which then forms the mixed thiolate/imidazole adduct upon addition of EMP [equations (2) and (3)]. Exposure of Fe^{II} $TMP(ImH)_2$ to air in the presence of excess EMP also produces the spectrum of the mixed complex, providing further evidence for its identification as an iron(III) species.

$$\mathrm{FeTMPOH + ImH \rightarrow FeTMP(ImH)(Im)} \quad (2)$$

$$\mathrm{FeTMP(ImH)(Im) + RSH \rightarrow FeTMP(ImH)(RS) + ImH} \quad (3)$$

The addition of 1-MeIm to a solution of FeTMP(EMP) in toluene does not result in the formation of a mixed adduct of $FeTMP^+$. Instead, reduction of iron(III) and formation of Fe^{II}-$TMP(1\text{-}MeIm)_2$ is observed, consistent with observations by other workers.[3] This difference in reactivity on addition of imidazole donors to FeTMP(EMP) can be explained by consideration of the stability of the iron(II) species which would be formed should reduction occur. $FeTMP(1\text{-}MeIm)_2$ is moderately stable in the presence of excess 1-methylimidazole even in air. In contrast, the bis-adduct of imidazole is oxidized rapidly upon exposure to air even in the presence of a large excess of imidazole. In the case of 1,2-dimethylimidazole, steric interactions between the 2-methyl hydrogen atoms and the electrons of the prophyrin ring prevent formation of a stable bisadduct of $Fe^{II}TMP$.[11] For those cases in which a stable iron(II) bisimidazole adduct can be formed, as in the case of 1-methylimidazole, reduction is observed upon addition of the imidazole donor to FeTMP(EMP). If a stable iron(II) bis-adduct cannot be formed, as in the case of imidazole and 1,2-dimethylimidazole, the iron(III) porphyrin mixed adduct is obtained.

Addition of O donors to FeTMP(EMP) also promotes the formation of stable mixed adducts as shown in Figure 2 for the reaction of FeTMPOH and EMP in tetrahydrofuran (THF). The general features of these complexes consist of a Soret absorption around 418 nm and a prominent visible band between 525 and 530 nm. A second visible band appears as a weak shoulder to the red of this band in THF. These spectra are also characteristic of six co-ordinate low-spin iron(III) porphyrins and are attributed to the formation of asymmetric complexes containing a S donor and an O donor. The reaction occurs in two distinct steps, producing initially a five co-ordinate spectrum with bands at 415.6, 496.3, 565.6, 645.6, and 675.0 nm, which is attributed to the monothiolate complex. Within 30 min this spectrum is completely converted to the six co-ordinate spectrum with bands at 418.1, 529.4, and 601.3 nm [equations (4) and (5)]. Addition of EMP to FeTMPOH in dimethylformamide (DMF) and in methanol produces similar spectra, which are assigned to the species FeTMP(SR)(DMF) and FeTMP(MeOH), respectively. (Table 1).

$$\mathrm{FeTMPOH + RSH \rightarrow FeTMPSR + H_2O} \quad (4)$$

$$\mathrm{FeTMPSR + THF \rightarrow FeTMP(SR)(THF)} \quad (5)$$

The role of hydroxide as a counter ion in the formation of the monothiolate complex is worthy of mention. No reaction is observed for the addition of EMP to FeTMPCl in the presence of added base. Presumably this is due to the tendency of the chloride ion to remain associated in nonco-ordinating solvents such as toluene. Similar behaviour has been observed for the formation of a dimercaptide complex from an iron(II) tetra-arylporphyrin chloride in dimethylsulphoxide or similarly co-ordinating solvents but not in toluene.[12] Hydroxide ion serves two purposes in the present study, functioning as a base for the deprotonation of the thiol ligand and as a readily dissociable anion.

So far, attempts to isolate the complexes described in this work have not been successful. While most of the complexes are stable for an hour or more in air, concentrated solutions of the monothiolate complex or the mixed adducts in the presence of excess EMP undergo gradual decomposition on standing for long periods. Further investigation of these complexes involves low temperature ESR studies and Mössbauer measurements for comparison with results which have been reported for unstable mixed ligand thiolate complexes.

Received, 4th October 1989; Com. 9/04245H

References

1 S. W. McCann, F. V. Wells, H. H. Wickman, T. N. Sorrell, and J. P. Collman, *Inorg. Chem.*, 1980, **19**, 621.

2 J. P. Collman, T. N. Sorrell, K. O. Hodgson, A. K. Kulshrestha, and C. E. Strouse, *J. Am. Chem. Soc.*, 1977, **99**, 5180.

3 S. C. Tang, S. Koch, G. C. Papaefthymiou, S. Foner, R. B. Frankel, J. A. Ibers, and R. H. Holm, *J. Am. Chem. Soc.*, 1976, **98**, 2414.

4 S. Koch, C. Tang, R. H. Holm, and R. B. Frankel, *J. Am. Chem. Soc.*, 1975, **97**, 914.

5 J. P. Collman, T. N. Sorrell, and B. M. Hoffman, *J. Am. Chem. Soc.*, 1975, **97**, 913.

6 S. Koch, S. C. Tang, T. H. Holm, R. B. Frankel, and J. A. Ibers, *J. Am. Chem. Soc.*, 1975, **97**, 916.

7 H. Ogoshi, H. Sugimoto, and Z. Yoshida, *Tetrahedron Lett.*, 1975, **27**, 2289.

8 R. Cheng, L. Latos-Grazynski, and A. L. Balch, *Inorg. Chem.*, 1982, 2412.

9 R. Quinn, M. Nappa, and J. S. Valentine, *J. Am. Chem. Soc.*, 1982, **104**, 2588.

10 E. McCandlish, A. R. Miksztal, M. Nappa, A. Q. Sprenger, J. S. Valentine, J. D. Stong, and T. G. Spiro, *J. Am. Chem. Soc.*, 1980, **102**, 4268.

11 J. P. Collman and C. A. Reed, *J. Am. Chem. Soc.*, 1973, **95**, 2048.

12 K. B. Nolan, *J. Chem. Soc., Chem. Commun.*, 1986, 760.

13 C. A. Tyson, J. D. Lipscomb, and I. C. Gunsalus, *J. Biol. Chem.*, 1972, **247**, 5777.

14 F. Mitani and S. Horie, *J. Biochem. (Tokyo)*, 1969, **66**, 139.