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Synthesis and Spectroscopic Properties of a Five Coordinate Tetrafluorophenylthiolato Iron II 'Picket Fence' Porphyrin Complex and its Carbonyl and Dioxygen Adducts: Synthetic Analogs for the Active Site of Cytochromes P 450

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A synthetic analog for the active site of cytochromes P 450 in the oxy state, $[Fe(O_2)(TP_{piv}P)SC_6HF_4]^-$, *1* was recently obtained by reaction of O_2 with a chlorobenzene solution of $Fe(TP_{piv}P)$ and $[K\subset 222][SC_6HF_4]$ [1]. *1* was characterized by UV and IR (solutions) and Mössbauer (solid state) spectroscopy. Surprisingly, the visible spectrum of the five coordinate starting material in chlorobenzene was not consistent with known spectral regions for other thiolato iron II porphyrin anions [2–6]. The precursor to *1* was indeed absorbing at 446 nm, while all other thiolato complexes display a Soret absorption near 420 nm. We now show that, due to chloride impurities in the cryptand used, this precursor was a five coordinate iron (II) chloro complex, $[FeTP_{piv}PCl]^-$. Its structure and spectroscopic properties are reported along with the synthesis, structure and spectral characterization of the actual precursor to the oxy complex *1*, $[Fe(TP_{piv}P)SC_6HF_4]^-$.

The initially reported synthesis employed zinc amalgam reduction in chlorobenzene of $Fe(TP_{piv}P)Cl(Br)$ [7] (0.088 mmol) followed by addition of a two-fold excess of KSC_6HF_4 cryptated with commercial unpurified 222 cryptand. The resulting solutions display visible absorptions at 446, 573 and 614 nm [1]. Single crystals were obtained by slow diffusion of pentane into these solutions. Their solid state UV spectrum is identical with those of the solutions. Analysis of the crystal structure showed the absence of thiolate and ligation of a chloride atom to iron (see below), the product being $[Fe(TP_{piv}P)Cl]^-[K\subset 222]$ C_6H_5Cl, *2*. Attempts to repurify all solvents and reagents and the use of a different solvent failed to yield a different species. Finally, the 222-cryptand was carefully purified and repetition of the above mentioned synthesis led to solutions with visible bands at 419, 530, 570 and 605 nm, consistent with the presence of an axial thiolate ligand [2, 6]: $[Fe(TP_{piv}P)SC_6HF_4][Na\subset 222]$, *3*. However, addition of pentane failed to yield a crystalline material and produced only oily precipitates. A different synthetic route has now been obtained: $Fe(TP_{piv}P)Cl$ (0.088 mmol) is reduced by zinc amalgam in benzene. The filtrate is transferred to a solution containing a five-fold excess of 18c.6 crowned sodium tetrafluorophenylthiolate [7]. Slow evaporation or diffusion of pentane yields crystalline $[Fe(TP_{piv}P)SC_6HF_4][NaC_{12}H_{24}O_6]$, *4*.

The spectral characteristics of the solid samples are similar to those of the solutions.

The Mössbauer properties of *2* and *3, 4* differ markedly [6]. Two samples of *2* have been submitted to analysis, one using non purified 222-cryptand in an attempt to form the thiolato complex, the other by direct synthesis from KCl. They both display the same Mössbauer parameters, *i.e.* isomer shift δ = 1.01 mm s^{-1} quadrupole splitting ΔE_Q = 4.36 mm s^{-1}, and line width Γ = 0.31 mm s^{-1} at 77 K, with standard deviations of ±0.02 mm s^{-1}. The isomer shift is given with respect to α-Fe at room temperature. The observed ΔE_Q value of *2* is the largest ever reported for a five coordinate high spin iron(II) derivative and exceeds greatly the values observed for the corresponding thiolato compounds [8]; its temperature dependence is practically negligible in the range between 4.2 and 215 K. The Mössbauer parameters for *4*, on the other hand, are close to the values previously reported [1], namely δ = 0.82, ΔE_Q = 2.37 and Γ = 0.27 mm s^{-1} (±0.02 mm s^{-1}) at 85 K. At 77 K, the parameters for *3* are: δ = 0.80, ΔE_Q = 2.36, Γ = 0.32 mm s^{-1}. However, the temperature dependence of the two samples *3, 4,* differs (Fig. 1). The ΔE_Q of *4* shows little variation while that of *3* has a more pronounced dependence. This difference is quite surprising and not entirely understood at present, but may originate from a difference in molecular structure: in the case of *4*, a crystal structure analysis has shown a strong chelation of sodium by one of the pivalamide arms (see below). Compound *4* can be carbonylated or oxygenated both in solution or in the solid state. The visible spectrum of the carbonyl adduct displays the usual hyperporphyrin spectrum with bands at 387, 451 and 559 nm, ν(CO)(IR) = 1956 cm^{-1} in benzene, (1942 cm^{-1} in the solid state). The Mössbauer parameters obtained at 4.2 K (δ = 0.30, ΔE_Q = 0.56, Γ = 0.29 mm s^{-1} (±0.02 mm s^{-1}) are

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TABLE I. Crystal and Data Collection Parameters for *2* and *4*.

	$[Fe(TP_{piv}P)Cl][KC_{18}H_{36}N_2O_6]C_6H_5Cl$ *2*	$[Fe(TP_{piv}P)SC_6HF_4][NaC_{12}H_{24}O_6]$ *4*
a, Å	23.023	13.158
b, Å	21.559	27.143
c, Å	18.232	25.333
β, deg	100.85	98.20
Z	4	4
Space group	*P*21/*n*	*P*21/*c*
Radiation	CuKα	CuKα
θ limits	3–57	3–56
Scan mode	Flying step	Flying step
Reflections collected	12500	11770
Reflections with $\sigma(I)/I < 0.33$	5318	5662
p (Ibers weighting scheme)	0.08	0.08
Temperature factor refinement	anisotropic for all non hydrogen atoms	anisotropic only for iron, sulfur and porphyrin core
R (present value)	0.072	0.14

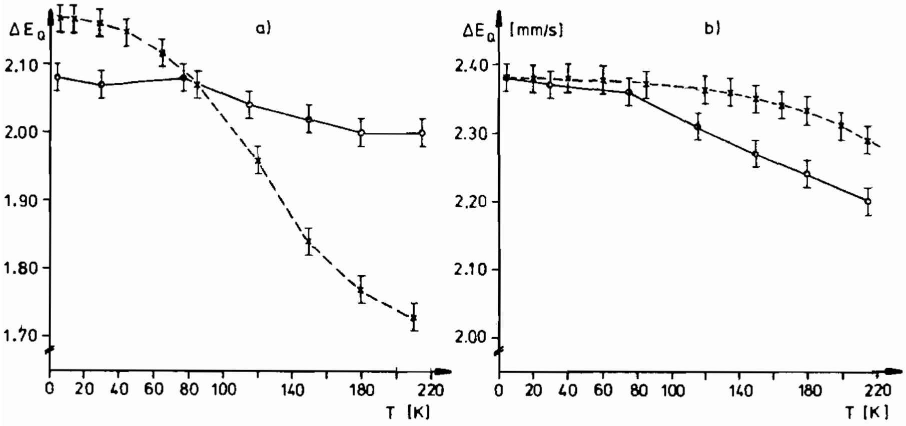

Fig. 1. a. Temperature dependence of quadrupole splittings for the oxy adducts, $[Fe(O_2)SC_6HF_4TP_{piv}P][Na\subset 18\text{-crown-}6]$, *5* (dashed line) and $[Fe(O_2)(SC_6HF_4)TP_{piv}P][Na\subset 222]$, *6* (solid line). b. Temperature dependence of quadruple splittings for five coordinate $[Fe(SC_6HF_4)TP_{piv}P][Na\subset 222]$, *3* (solid line) and $[Fe(SC_6HF_4)TP_{piv}P\text{-}[Na\subset 18\text{-crown-}6]$, *4* (dashed line).

typical of low spin iron(II). A powdered sample of *4* (120 mg) was exposed to O_2 (1.5 bars) at 273 K for 60 mn. The resulting Mössbauer spectrum (Fig. 2) shows that about 97% oxygen uptake has occurred. The Mössbauer parameters of the new product $[Fe(O_2)(SC_6HF_4)TP_{piv}P][NaC_{12}H_{24}O_6]$, *5* are at 4.2 K: $\delta = 0.32$, $\Delta E_Q = 2.16$, $\Gamma = 0.29$ mm s^{-1} (±0.02 mm s^{-1}). The parameters for the analogous complex $[Fe(O_2)(SC_6HF_4)TP_{piv}P][Na\subset 222]$, *6* obtained by oxygenation of *3* are at 4.2 K: $\delta = 0.29$, $\Delta E_Q = 2.08$, $\Gamma = 0.32$ mm s^{-1} (±0.02 mm s^{-1}). Their ΔE_Q temperature dependences are shown in Fig. 1. An intriguing point is the reversal of behavior in temperature dependence which is now large for compound *5* obtained with $[Na(18\text{-crown-}6)]^+$ and very small for *6* obtained with $[Na\subset 222]^+$. Thus the Mössbauer parameters of the dioxygen adducts *5* and *6* are very close to those reported for oxy $P450_{CAM}$ except that *6* has the same type of temperature dependence as the protein whereas the temperature dependence of *5* is clearly different.

The spectral properties of *5* are close to those previously reported [1]. *5* presents UV absorptions at 360, 426, 500 and 610 nm. Oxygenation of single crystals of *4* in the solid state yields $\nu(^{16}O_2)$ at 1141 cm^{-1} ($\nu^{18}O_2$) 1075 cm^{-1} [1]. These values indicate

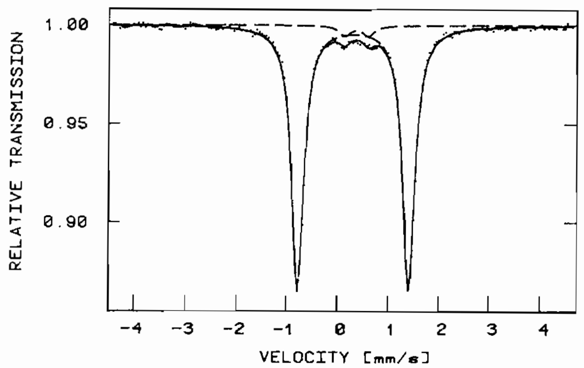

Fig. 2. Mössbauer spectrum (4.2 K) of $[Fe(O_2)(SC_6HF_4)TP_{piv}P][Na\subset 18\text{-crown-}6]$, *5* obtained by oxygenation at 273 K for 60 mn of a powdered sample of the five coordinate ferrous material *4*. (Oxygenation was achieved to about 97%). (Mössbauer spectra were accumulated with a standard apparatus in the constant acceleration mode with a Co/Rh (*ca.* 50 mCi) source. Isomeric shifts are given with respect to αFe at room temperature).

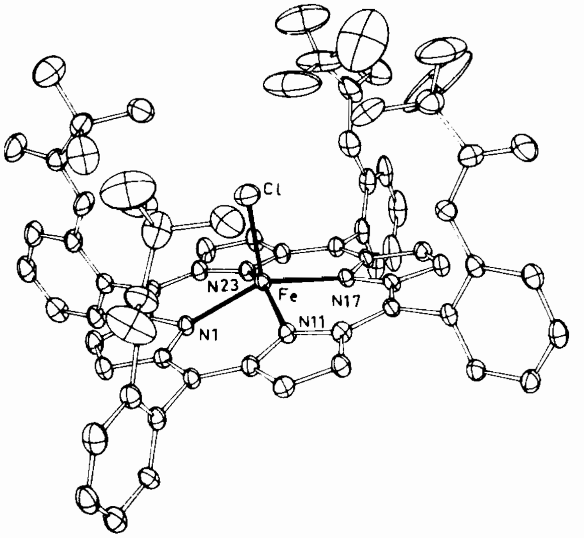

Fig. 3. ORTEP drawing of $[Fe(SC_6HF_4)TP_{piv}P]$ present in *2*.

a bent end-on bonded stereochemistry for the $Fe-O_2$ moiety. This result is confirmed by an X-ray study of a related O_2 adduct $[Fe(O_2)SC_6HF_4(TP_{piv}P)][K\subset 222]_2[SC_6HF_4][C_6H_5Cl\cdot(H_2O)_x]$ [8].

Crystal structures for both *2* and *4* have been determined. Crystal data for both complexes are assembled in Table I. An ORTEP drawing of $[FeTP_{piv}PCl]^-$ is shown in Fig. 3. Iron is five coordinate.

The chloride ion lies in the axial position inside the cavity formed by the pivalamide arms of the picket fence porphyrin. The Fe–Cl bond of 2.301(2) Å is approximately 0.09 Å longer than that in several chloro-iron(III) porphyrin complexes [10, 11]. The mean value of the $Fe-N_p$ distances is 2.108 (±0.015) Å and is the longest reported so far for such an iron $II-N_p$ bond. The consequence is that the iron atom lies above the $4N_p$ mean plane by 0.534 Å and 0.593 Å out of the 24 atom-core mean plane. The net doming (0.059 Å) is small and only slightly larger than that present in high-spin mercapto iron(II) porphyrins [6–8]. The displacement of iron out of the 4N plane is the largest observed so far in high spin iron(II) porphyrin derivatives [12].

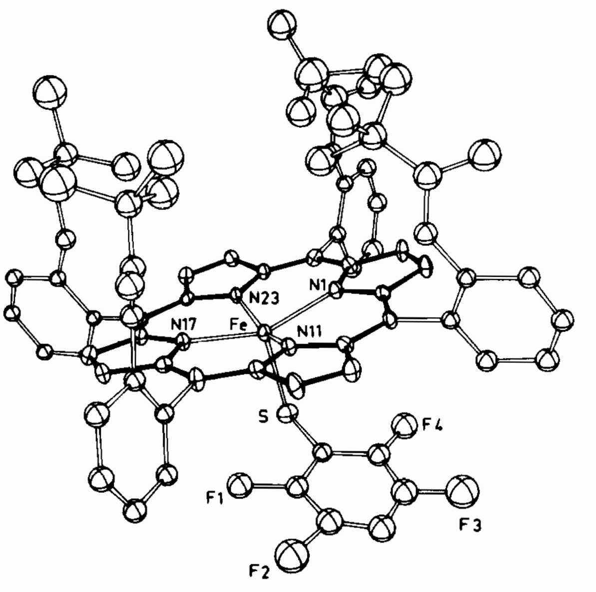

Fig. 4. ORTEP drawing of $[Fe(SC_6HF_4)TP_{piv}P]^-$ present in *4*.

The stereochemistry of *4* is shown in Fig. 4. Again, iron is five coordinate but now, the thiolato ligand is bonded to iron on the non protected face of the picket fence porphyrin, as was hoped, thus leaving an empty molecular cavity. At the present stage of refinement, the FeS bond distance (2.370(3) Å) is similar to that found in several other thiolato iron (II) porphyrinato anions [6]. The Fe–S–C angle is close to 104°. The mean value of the $F-N_p$ distances is 2.076 (±0.020) Å.

The displacement of iron out of the $4N_p$ plane (0.42 Å) would appear slightly smaller than in the other compounds studied so far. A surprising feature of this structure was the finding of a very strong interaction of sodium with a carbonyl group of the picket arms. The $C{=}O\cdots Na^+$ distance is 2.33 Å, shorter than any of the 18-crown-6 oxygen to sodium distances (range from 2.46 Å to 2.66 Å).

The spectral properties displayed by the tetrafluorophenylthiolato derivatives of picket fence iron porphyrin provide convincing evidence, by comparison with those known for the reduced, carbonylated and oxygenated states of cytochromes P450, that a cysteinate sulfur atom is the axial ligand of iron in all these states. Thus, cysteinate sulfur ligation is most probably present throughout the catalytic cycle of these cytochromes. This result is in agreement with those obtained by spectroscopic techniques on cobalt substituted $P450_{CAM}$ [13] and the corresponding synthetic analogs [14].

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