lized by immobilization. For example, **6a** is stable in the crystalline state, and **6i** in which the imidazoie ligand is N-bonded to cross-linked polystyrene is unchanged after prolonged storage as a solvent-free solid at 25°. These results could provide an explanation for the membrane stabilization of P-450's.[12]

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(3) The following abbreviations are used in this paper: ⋙CH = a hydrocarbon substrate, ⋙COH = hydroxylated product, TPP = *meso*-tetraphenylporphyrin, N-MeIm = *N*-methylimidazole, THT = tetrahydrothiophene, THF = tetrahydrofuran, cam = camphor, Ⓟ-Im = polystyrene-bonded imidazole.[4]

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(5) Actually, this substrate bound ferric form **2** exhibits an equilibrium between high and low spin forms.[2] We suggest the possibility that this equilibrium arises from competitive coordination of the camphor carbonyl.

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(7) During the course of our studies, we learned of similar work by R. H. Holm to whom we are indebted for making his results available to us prior to publication: S. Koch, S. C. Tang, R. H. Holm, and R. B. Frankel, *J. Amer. Chem. Soc.*, following paper; J. C. Tang, S. Koch, R. H. Holm, R. B. Frankel, and J. A. Ibers, *ibid.*, following paper.

(8) These compounds have been characterized by elemental analysis. These results were provided to the referees. A single-crystal X-ray diffraction structural analsis of **6a** is in progress.

(9) (a) All such solutions of **5** exhibit an additional unidentified ferric porphyrin signal at $g = 6$ whose intensity increases slowly with time. In freshly prepared samples this impurity is <10%. (b) With the exception of **6a**, **e**, **g**, and **h** (determined at 77°K) all ESR spectra in the present work were determined at both 77 and 20°K and showed no apparent change indicating the absence of a spin equilibrium such as that reported[2] for **1** and **2** (see ref 6). (c) Axial bases were used in excess to form **6b–f**, especially using camphor to form **6e**. This may explain the apparent discrepancy between our work and that of Holm.

(10) J. A. Peterson and B. W. Griffin, *Drug Metab. Dispos.*, **1**, 14 (1973).

(11) Competition experiments show that N-MeIm is bound preferentially over THF, THT, or cam. This raises the question as to how camphor substrate could replace a histidyl imidazole in going from **1** to **2**.

(12) In P-450$_{cam}$ which is not membrane bound the protein may afford such protection as is found in oxygenated hemoglobin.

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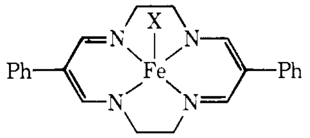
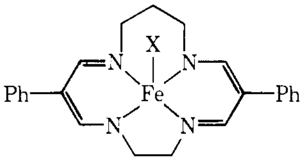
The [$Fe^{III}N_4SR$] Coordination Unit. Synthesis and Ground State Electronic Properties of Macrocyclic Ferric Thiolates

Sir:

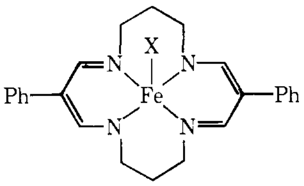
The structural, electronic, and reactivity properties of natural and synthetic Fe(II, III) porphyrin complexes are significantly dependent upon the interactions of heme-iron with its axial ligand(s). In this regard the generalized [FeN_4S] coordination unit of idealized tetragonal microsymmetry is of particular current interest because of its possible occurrence in one or more of the reaction states of cytochrome P-450 enzymes.[1] In, for example, the P-450 camphor hydroxylase system, four reaction states of the enzyme have been identified[2] and the occurrence of sulfur-ligated forms is a matter of active speculation.[1,2] Although there have been reports of the electronic absorption and EPR spectra[1-6] of complexes described as ferric porphyrin thiolates, the great majority of these species were generated in situ, usually in the presence of a nitrogenous base, and were not isolated or otherwise characterized. In order to probe the properties of this donor atom arrangement, we report here and in the following communication[7] the synthesis and certain ground state electronic features of species containing the [$Fe^{III}N_4SR$] unit, previously unknown in stable isolable complexes.[8] This work has utilized both porphyrin and other types of synthetic diprotic macrocycles[9] as N_4 ligands as a means of detecting any modifying effects of supporting ligand structure on the properties of this unit.



Fe(6565)X
X = OAc (**1a**)
SPh (**1b**)
Br (**1c**)



Fe(6566)X
X = OAc (**2a**)
SPh (**2b**)
Br (**2c**)



Fe(6666)X
X = OAc (**3a**)
SPh (**3b**)
SCH$_2$Ph (**3c**)
Br (**3d**)
OCOPh (**3e**)

Reaction of 14-, 15-, and 16-membered metal-free bis(β-iminoamine) macrocycles[9] with ferrous and basic ferric acetate in hot DMF solution gave in good yield the corresponding Fe(II) (X absent) and Fe(III) macrocycles (X = OAc) **1a–3a**,[10] respectively, which serve as precursors for thiolate complexes. The latter were synthesized by the substitution reaction (1) and the oxidative addition reaction

$$Fe^{III}N_4OAc + RSH \longrightarrow Fe^{III}N_4SR + HOAc \tag{1}$$

$$Fe^{II}N_4 + \tfrac{1}{2}RSSR \longrightarrow Fe^{III}N_4SR \tag{2}$$

(2). Both reactions yield **1b–3b** while **3c** was obtained by the first method. In a synthesis typical of reaction 1, 1.1 equiv of benzenethiol was added to an ethanol suspension of 1.0 equiv of **1a**. After 1 hr reaction time at 25°, filtration, and recrystallization (DMF-methanol, 25°), **1b** was obtained in 90% yield as brown crystals. As an example of reaction 2, Fe(6566) and diphenyl disulfide were allowed to react in DMF solution for 1 hr at 25°. Work-up and recrystallization afforded black crystalline **2b** (50%). The reactive Fe(II) macrocycles also undergo facile oxidative addition with other reagents including halogens and dibenzoyl peroxide, affording the complexes **1c**, **2c**, **3d**, and **3e**. Ferric porphyrin thiolates were most conveniently prepared in high analytical and magnetic[10] purity by the cleavage of μ-oxo dimers with relatively acidic thiols[11] in toluene solution at

Table I. Electronic Properties of $Fe^{(III)}N_4SR$ Complexes

Complex		Spin state	Magnetism		Isomer shift $(\delta)^d$	Quadrupole splitting $(\Delta E_Q)^d$	g values^e
			μ (BM)^a	θ^b			
Fe(6565)SPh	**(1b)**	$S = 1/2$	1.95	g	0.04	3.60	2.11, 2.04, 2.01
Fe(6566)SPh	**(2b)**	$S = 3/2$	3.94	3.0	g	g	f
Fe(6666)SPh	**(3b)**	$S = 3/2$	4.17	5.9^c	0.26	1.93	f
Fe(6666)SCH_2Ph	**(3c)**	$S = 5/2$	5.88	2.0	0.35	0.71	7.5, 4.5, 1.9
Fe(OEP)SPh	**(4)**	$S = 5/2$	5.87	g	0.31	0.49	7.2, 4.7, 1.9
Fe(OEP)(SC_6H_4-p-NO_2)	**(5)**	$S = 5/2$	5.92	g	0.32	0.66	g

[a] Calculated from ambient temperature data using the Curie law. [b] From least-square fits of the data (20–295°K) to $\chi_M^{corr} = C/(T + \theta)$. [c] From data at 20–200°K; small departure from Curie behavior at higher temperatures. [d] In mm/sec at 300°K; δ relative to Fe metal. [e] Toluene glass at ~95°K. [f] More complicated spectra, to be considered in a subsequent report. [g] Not measured.

25°, reaction 3. Very pure dimers are readily obtainable by chromatography[12,13] and did not lead to high-spin impurities in the reaction products.

$$[Fe(P)]_2O + 2RSH \longrightarrow 2Fe(P)SR + H_2O \qquad (3)$$

Thus, reaction of the octaethylporphyrinato dimer $[Fe(OEP)]_2O$[12] with an ca. sixfold excess of benzenethiol and p-nitrobenzenethiol in toluene afforded Fe(OEP)SPh (**4**) and $Fe(OEP)SC_6H_4NO_2$ (**5**), which separated from the reaction solution as purple-black crystals in 90% yield. A corresponding complex of protoporphyrin IX dimethyl ester is described elsewhere.[7] With both OEP and PPIX dimers alkyl thiols effected reduction to Fe(II) and no Fe(III) thiolate complexes could be isolated, in contrast to the stability of **3c**.

Coordination units of the [FeN_4X] type are found in Fe(III) porphyrins (X = halide, pseudohalide, RCO_2, OR) which without exception are high spin[3,14] with tetragonal pyramidal stereochemistry.[15] Data in Table I for sulfur-ligated **4** and **5**, described more fully in the following paper,[7] include EPR[6] and Mössbauer[16] parameters characteristic of high-spin Fe(III) porphyrins and suffice to show that these complexes fall into that category. However, the remaining data amply demonstrate that high-spin behavior is not an invariant property of the [$Fe^{III}N_4SR$] unit. As shown by magnetic susceptibility results, suitable variation of R and macrocycle ring size affords stabilization of all three possible spin states of Fe(III). The zero-field Mössbauer spectra of these complexes consist of a simple quadrupole doublet with little variation in δ and ΔE_Q from 4.2°K to room temperature. Parameters of **3c** (especially δ) are similar to **4** and **5** and the high-spin assignment is supported by the large magnetic hyperfine interaction (ca. −450 kOe at 4.2°K) induced by the applied field H_0 = 80 kOe. Parameters for **1b** differ markedly from those of high-spin species with δ typical of low-spin Fe(III),[17] but ΔE_Q is unusually, but not uniquely,[18] large for this spin state. The low-spin assignment is also consistent with the EPR spectrum and the relatively small hyperfine interaction (ca. −70 kOe, H_0 = 80 kOe, 4.2°K). For the usual ferric core polarization hyperfine field of ca. −200 kOe/μ_B, one expects ca. −100 kOe for the $S = \frac{1}{2}$ case. Values of δ and ΔE_Q for **3b** are intermediate between the high- and low-spin cases as is the hyperfine interaction (ca. −270 kOe, preceding conditions, vs. ca. −300 kOe predicted for $S = \frac{3}{2}$), which is consistent with the spin assignment. Spin quartet ground states have been established previously for $Fe(S_2CNR_1R_2)_2X$ complexes.[19-21]

From the foregoing results and related observations, the following characteristics of macrocyclic five-coordinate Fe(III) thiolates emerge. (i) Porphyrin complexes are high spin and appear sufficiently stable for isolation only when containing the more electronegative (usually aromatic) thiolate ligands. (ii) Magnetic properties of the [$Fe^{III}N_4SR$] unit are dependent upon both the nature of R (**3b, 3c**) and supporting ligand structure. At parity of R (**1b–3b**) increasing macrocycle ring size progressively favors stabilization of the higher spin states, an effect presumably due to increasingly larger dimensions (and possibly deviations from coplanarity) of the N_4 "hole" subunit and attendant decreases in ligand field strength.[22] The series **1b, 2b, 3c** encompassing three spin states is currently unique among tetragonal Fe(III) systems. (iii) The quartet ground state, decidedly uncommon for d^5 ions and previously confined mainly to $Fe(S_2CNR_1R_2)_2X$,[19,20] is readily achieved in stable macrocyclic complexes. Examples other than those in Table I include Fe(6565)X, X = OAc, Cl, Br, I (3.88–3.98 BM) and Fe(6566)Br (4.09 BM); Fe(6666)X, X = OAc, $PhCO_2$, are high-spin (5.88 BM).[23] These results show that the axial ligand field component generated by SPh is sufficiently larger than that due to X = halide, RCO_2 to effect a spin-state difference in the 6565 and 6666 series. All 6566 complexes examined thus far possess intermediate spin.

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(23) Magnetic moments at ~25°.

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Ferric Porphyrin Thiolates. Possible Relationship to Cytochrome P-450 Enzymes and the Structure of (*p*-Nitrobenzenethiolato)iron(III) Protoporphyrin IX Dimethyl Ester

Sir:

Four distinct reaction states of the cytochrome P-450 enzyme, each with characteristic electronic properties, have been identified in the *Pseudomonas putida* camphor hydroxylase system.[1-6] The possibility, in one or more reaction states, of axial sulfur ligation[1,7] to the iron protoporphyrin IX prosthetic group present in this[8] and other systems[9] has proved difficult to assess in the absence of known properties of fully characterized sulfur-bound iron porphyrins, which should serve as a guide to those developed by a [$\mathrm{FeN_4S}$] coordination unit present in the enzymes. The *P. putida* cytochrome has in addition to 6 Cys residues, 9 Met, 9 Tyr, and 12 His,[1,10] potentially affording the units [$\mathrm{FeN_4X}$], X = SR, OR, N(Im), one of which should apply to the high-spin component[1,4-6] of $\mathrm{Fe^{III}}$-P-450$_{\mathrm{cam}}$·S (substrate-bound). The low-spin component of this state and low-spin substrate-free $\mathrm{Fe^{III}}$P-450$_{\mathrm{cam}}$ are assigned six-coordinate geometry. The simple synthesis of Fe(III) porphyrin thiolates described in the preceding communication,[11] its ready extension to [$\mathrm{Fe^{III}N_4OR}$] analogs, and the availability of other pertinent data permit a more stringent examination of axial coordination[12] in oxidized reaction states than possible heretofore.

The title compound, Fe(PPIXDME)($\mathrm{SC_6H_4NO_2}$) (**1**), and Fe(PPIXDME)($\mathrm{OC_6H_4NO_2}$) (**2**)[13] were prepared from [Fe(PPIXDME)]$_2$O[14] and the corresponding thiol and phenol, respectively, in toluene solution.[11] Complex **1** crystallizes in triclinic space group C_i^1-$P\bar{1}$ with a cell of dimensions a = 13.596 (9) Å, b = 14.021 (4) Å, c = 13.307 (4) Å, α = 110.80 (6)°, β = 119.67 (6)°, γ = 62.62 (6)°, Z = 2, and V = 1930 Å^3. Observed and calculated densities are 1.377 and 1.35 (2) g/cm^3, respectively. At the present stage of isotropic refinement, based on 2557 unique data having $F_o^2 > 3\sigma(F_o^2)$ and including no absorption corrections or H atom contributions, the R index is 0.11 for 55 non-H atoms. The structure of the [$\mathrm{FeN_4SC}$] unit, shown in Figure 1, contains these features: the Fe atom appears slightly asymmetrically bonded to the four N atoms and is displaced out of the $\mathrm{N_4}$ (0.43) and 24 atom porphyrin (0.45 Å) mean planes toward the axial ligand (similar displacements are found in other high-spin Fe(III) porphyrins,[15] including hemin chloride,[15a] **3**); Fe-S-C = 101°; the phenyl ring forms dihedral angles of 11, 88, and 100° with the $\mathrm{N_4}$, FeN(1)N(3), and FeN(2)N(4) planes, respectively.

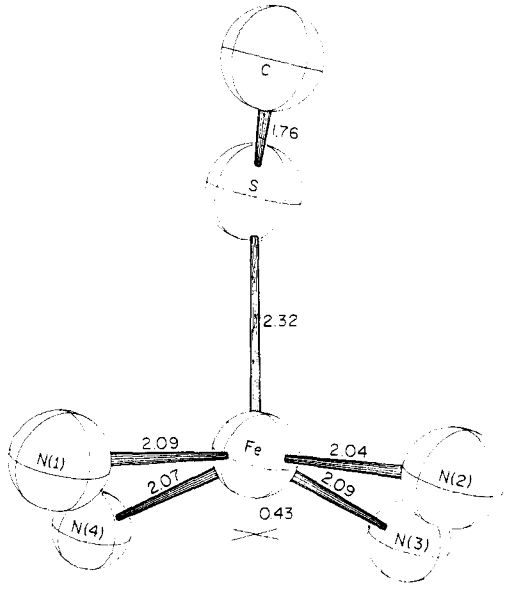

Figure 1. Perspective view of the inner coordination geometry of Fe(PPIXDME)$\mathrm{SC_6H_4NO_2}$ (phenyl ring omitted). Estimated standard deviations of bonded distances are 0.01 Å.

Magnetic properties **1** are consistent with its structure and include high-spin susceptibility behavior ($\chi_M^{\mathrm{corr}} = 4.412/(T + 3.2)$, 20–295°K) with μ = 5.90 BM at 295°K. For **2** μ = 5.90 BM (295°K). The symmetric quadrupole doublet in the Mössbauer spectrum of **1** at 4.2°K becomes increasingly asymmetric due to broadening of the higher velocity component as the temperature is raised, a behavior entirely similar to that observed and interpreted for **3**.[16] As with **3**[17] application of a strong magnetic field at low temperature induces a large magnetic hyperfine interaction (ca. −440 kOe, H_0 = 80 kOe, 4.2°K), expected for high-spin Fe(III).[11] Mössbauer parameters[18] (δ, ΔE_Q) are the following: **1**, 0.29, 0.70; **2**, 0.29, 0.67; **3**, 0.35, 0.75. These values are typical of high-spin Fe(III) porphyrins and those of **1** are close to the values for high-spin $\mathrm{Fe^{III}}$-P-450$_{\mathrm{cam}}$·S[5] (0.35, 0.79 mm/sec, ~200°K). However, as these and other results now reveal, Mössbauer parameters for high-spin complexes measured in zero magnetic field are insufficiently sensitive to distinguish axial sulfur ligands from X = OR,[19] N(Im),[20] and other groups.

The electronic spectra of **1** and **2** (Figure 2) display significant differences, particularly in the Soret and α-band (600–650 nm) regions. In the spectra of **2** and Fe(PPIXDME)OMe[21] the Soret band occurs at somewhat lower energy and the α-band is significantly blue-shifted compared to **1**. Further, in acid-met myoglobin and hemoglobin spectra[22] Soret and α-bands generally occur at ca. 405–410 and 623–635 nm with relative intensities different from that of **1**. Indeed, the spectrum of **1** is in very close agreement with those of high-spin $\mathrm{Fe^{III}}$-P-450$_{\mathrm{cam}}$·S ($\lambda_{\max}(\epsilon)$ = 391 (87), 646 nm (4.5 m*M*))[1-3] and microsomal high-spin P-450.[23] These results are considered to favor axial sulfur (S-Cys) over oxygen or nitrogen coordination in these high-spin cytochromes, with perhaps the most characteristic spectral feature of this ligation mode being the relatively weak α-band at ~646 nm.