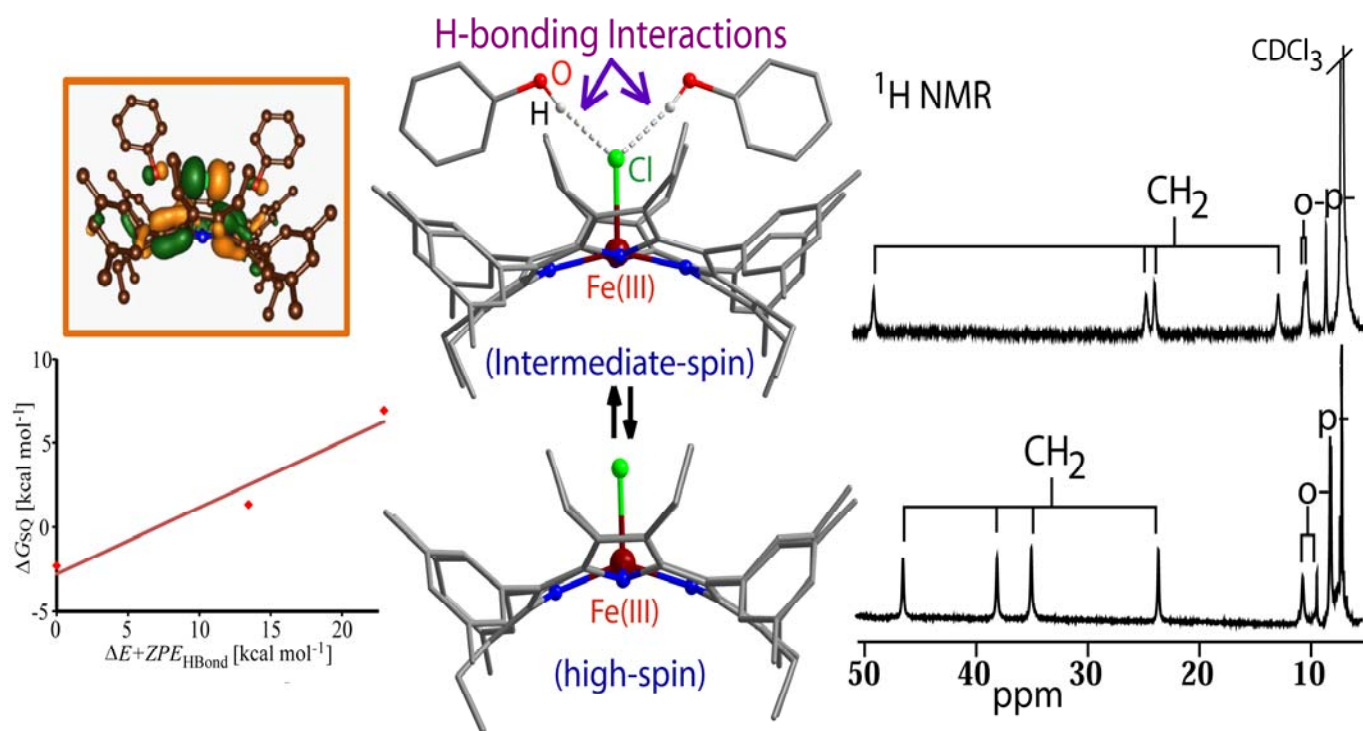


# Mono-Heme Cytochromes: Structure-Function Correlation

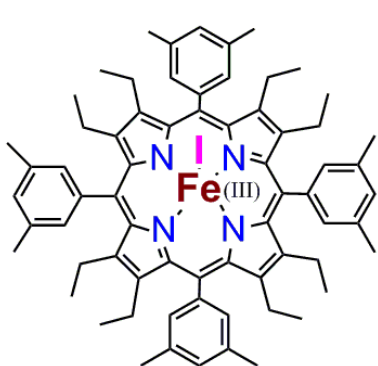
## ❖ H-bonding Interactions Trigger Spin-flip

We are currently engaged studying a wide range of bioinorganic and biological systems, all of which fall under the general theme of gaining a better understanding of the heme centers in heme proteins that are vital to the life of almost all living organisms. A key step in cytochrome P450 catalysis includes the spin-state crossing from low-spin to high-spin upon substrate binding and the subsequent reduction of the heme. Clearly, a weak perturbation in P450 enzymes triggers a spin-state crossing. However, the origin to the process whereby enzymes reorganize their active site through external perturbations, such as hydrogen bonding is still poorly understood. To gain insight, we have studied the impact of H-bonding interactions on the electronic structure of a five-coordinate iron(III)octaethyltetraarylporphyrin chloride. The spin state of the metal was found to switch reversibly between high ( $S = 5/2$ ) and intermediate-spin ( $S = 3/2$ ) just by the use of H-bonding. Our work highlights the possible effects and importance of H-bonding interactions in heme proteins. This is the first example of a synthetic iron(III) complex that can reversibly change its spin-state between high and intermediate state through weak external perturbations.

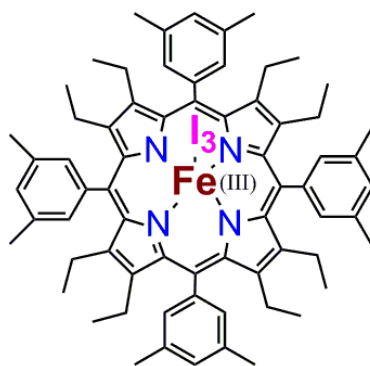


## ❖ Controlled Generation of (Porphyrinato)Iron(III) Iodide, Tri-iodide and Oxidized complex

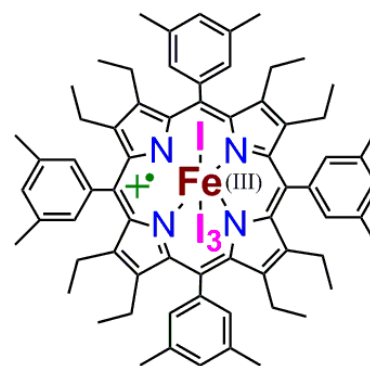
Three iron(III)porphyrinato complexes have been isolated just by varying iodine concentration which eventually form admixed-intermediate (iodo complex), pure intermediate (tri-iodide complex) and high-spin (1e-oxidized complex) states of iron where iodide and/or tri-iodide used as axial ligands. Computational calculations clearly support the experimentally assigned spin state.



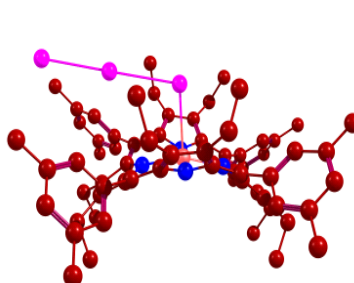
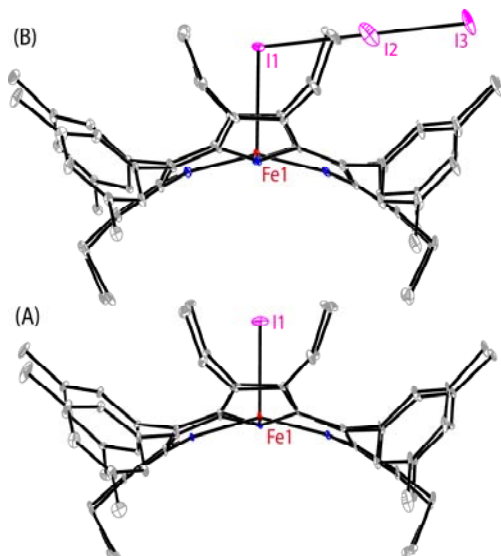
Spin: admixed-intermediate



intermediate



high



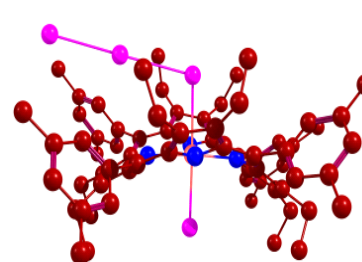
$$r_{\text{Fe-I}} = 2.951 [2.877]$$

$$r_{\text{Fe-Np}} = 1.970 [2.062]$$

$$\Delta_{24}^{\text{Fe}} = 0.22 [0.42]$$

$$\Delta G_{\text{SQ}} = +10.63$$

$^4\mathbf{3} [^6\mathbf{3}]$



$$r_{\text{Fe-I}} = 2.730 [2.869]$$

$$r_{\text{Fe-I3}} = 2.911 [3.777]$$

$$r_{\text{Fe-Np}} = 1.975 [2.070]$$

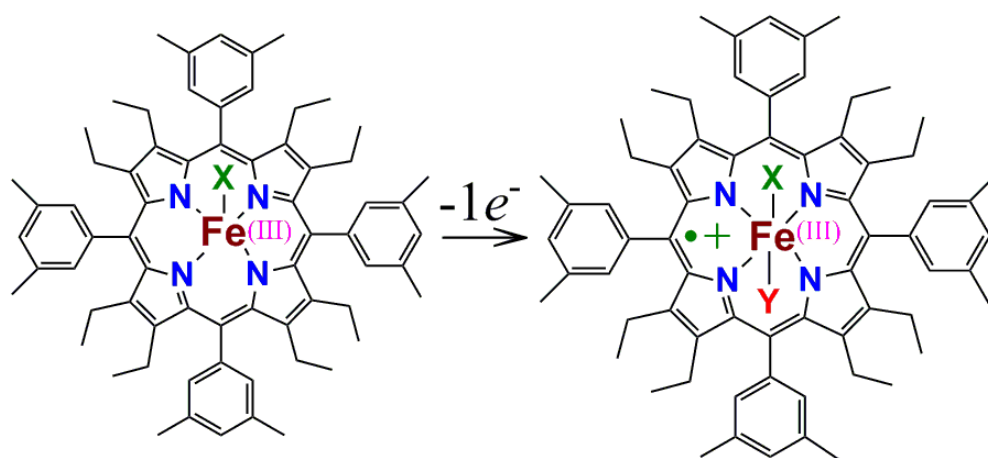
$$\Delta_{24}^{\text{Fe}} = 0.03 [0.03]$$

$$\Delta G_{\text{SQ}} = -6.7$$

$^3\mathbf{4} [^5\mathbf{4}]$

## ❖ Spin Modulation Using Axial Coordination and Their $\pi$ -Cation Radicals

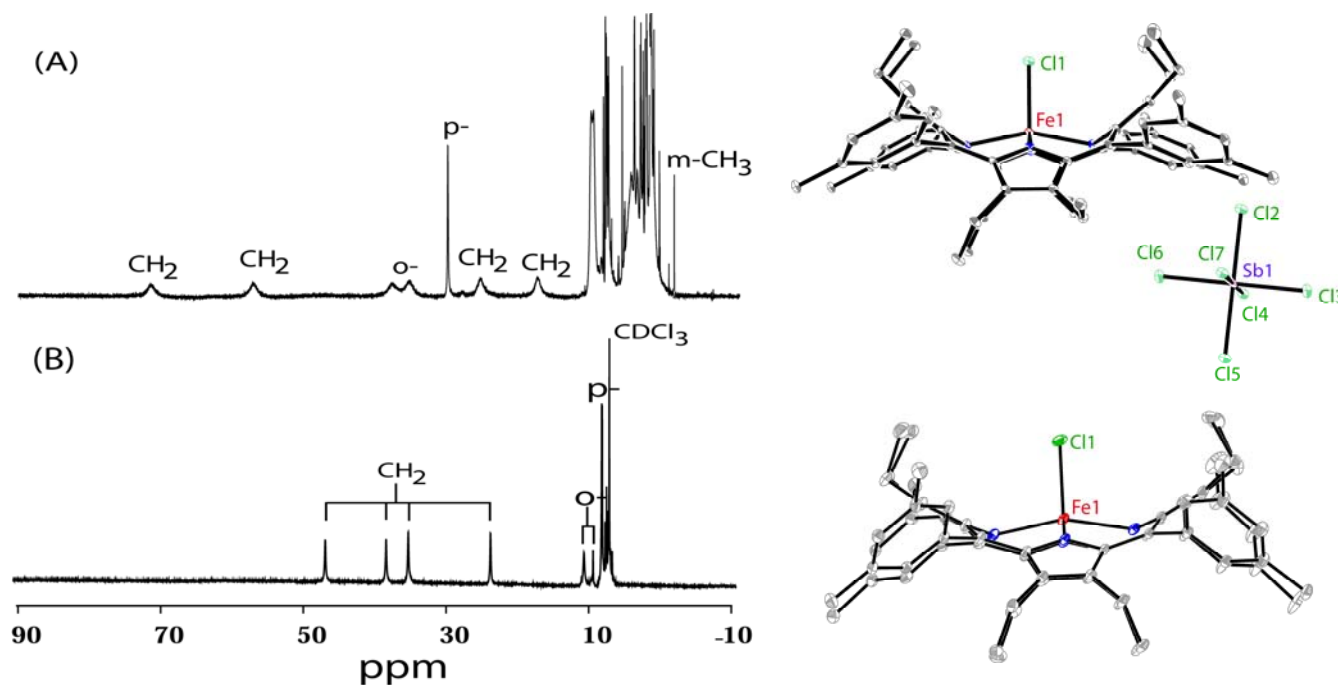
A series of five-coordinate Fe(III)octaaryltetraphenylporphyrins varying axial ligand field strength and their 1e-oxidized complex have been synthesized and characterized. The molecular structures and their spectroscopic properties including metal spins have been scrutinized..

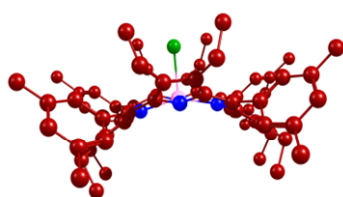


**X:** Cl, I, I<sub>3</sub>, ClO<sub>4</sub>, SO<sub>3</sub>CF<sub>3</sub>

**Y:** SbCl<sub>6</sub>, I<sub>3</sub>, ClO<sub>4</sub>, SO<sub>3</sub>CF<sub>3</sub>

<sup>1</sup>H NMR in CDCl<sub>3</sub>:



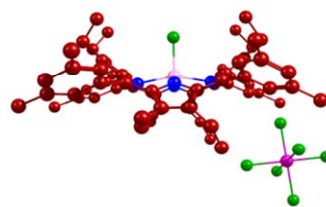
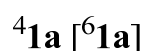


$$r_{\text{Fe-Cl}} = 2.439 [2.378]$$

$$r_{\text{Fe-Np}} = 1.975 [2.056]$$

$$\Delta_{24}^{\text{Fe}} = 0.31 [0.49]$$

$$\Delta G_{\text{HS/IS}} = -2.24$$

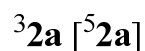


$$r_{\text{Fe-Cl}} = 2.384 [2.334]$$

$$r_{\text{Fe-Np}} = 1.962 [2.050]$$

$$\Delta_{24}^{\text{Fe}} = 0.31 [0.47]$$

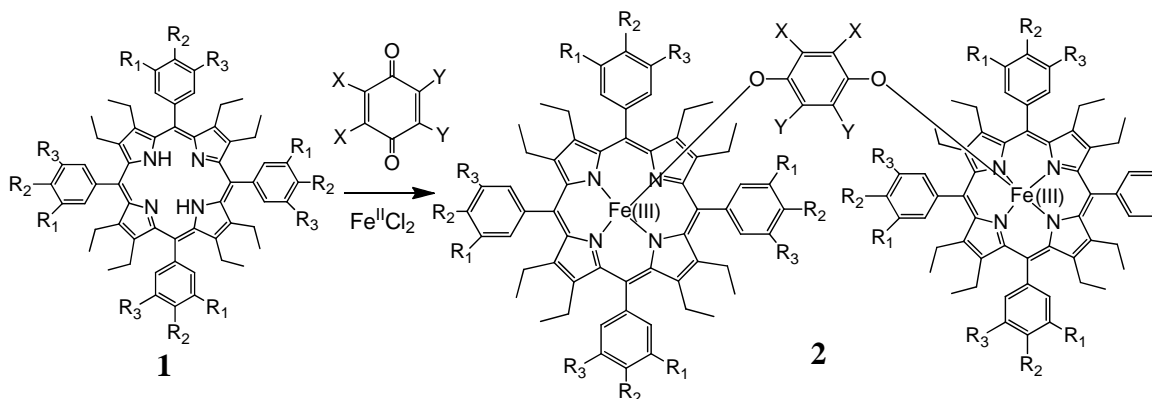
$$\Delta G_{\text{HS/IS}} = -3.63$$



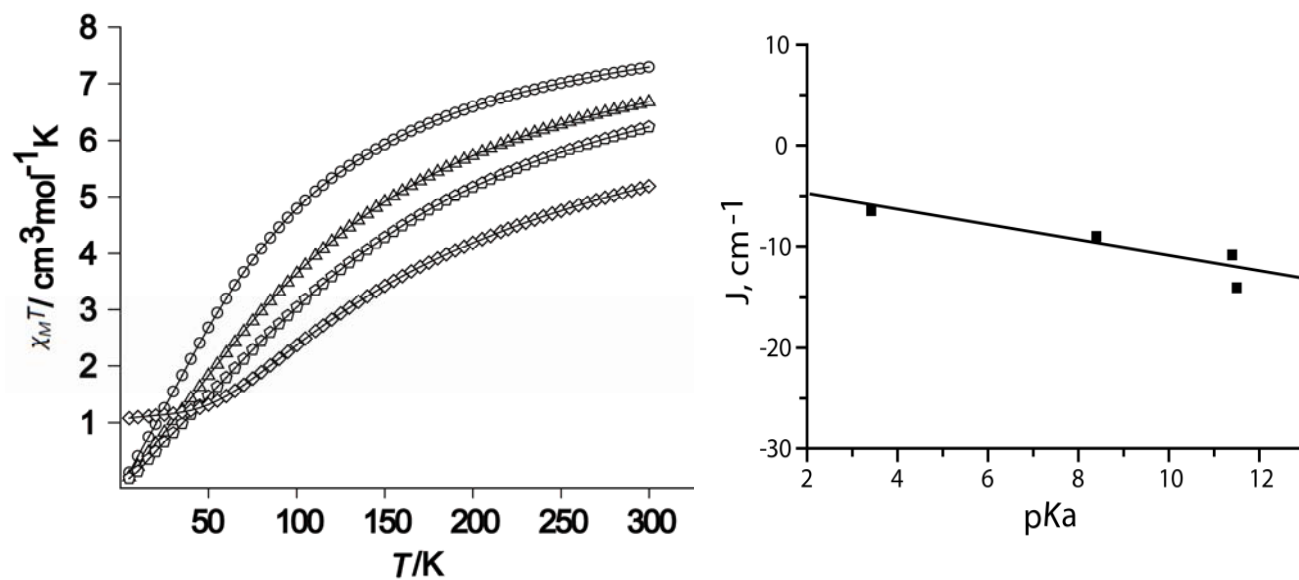
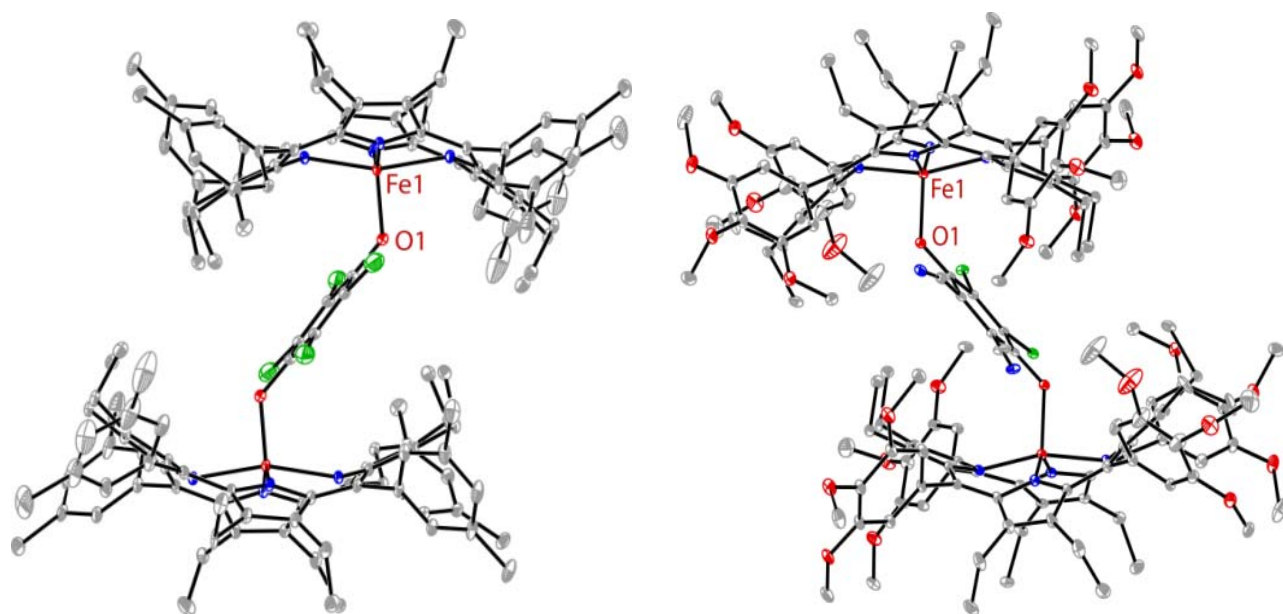
UB3LYP optimized geometries of  ${}^{4,6}\mathbf{1a}$ , and  ${}^{3,5}\mathbf{2a}$  with bond lengths ( $r$ ) in Å.  $\Delta_{24}^{\text{Fe}}$  is the displacement of the metal from the least-square plane of the  $\text{C}_{20}\text{N}_4$  porphyrinato core. Free energies  $\Delta G_{\text{HS/IS}}$  are relative to the intermediate spin state in  $\text{kcal mol}^{-1}$ .

## ❖ Exploring the Role of Bridge in the Electronic Communication

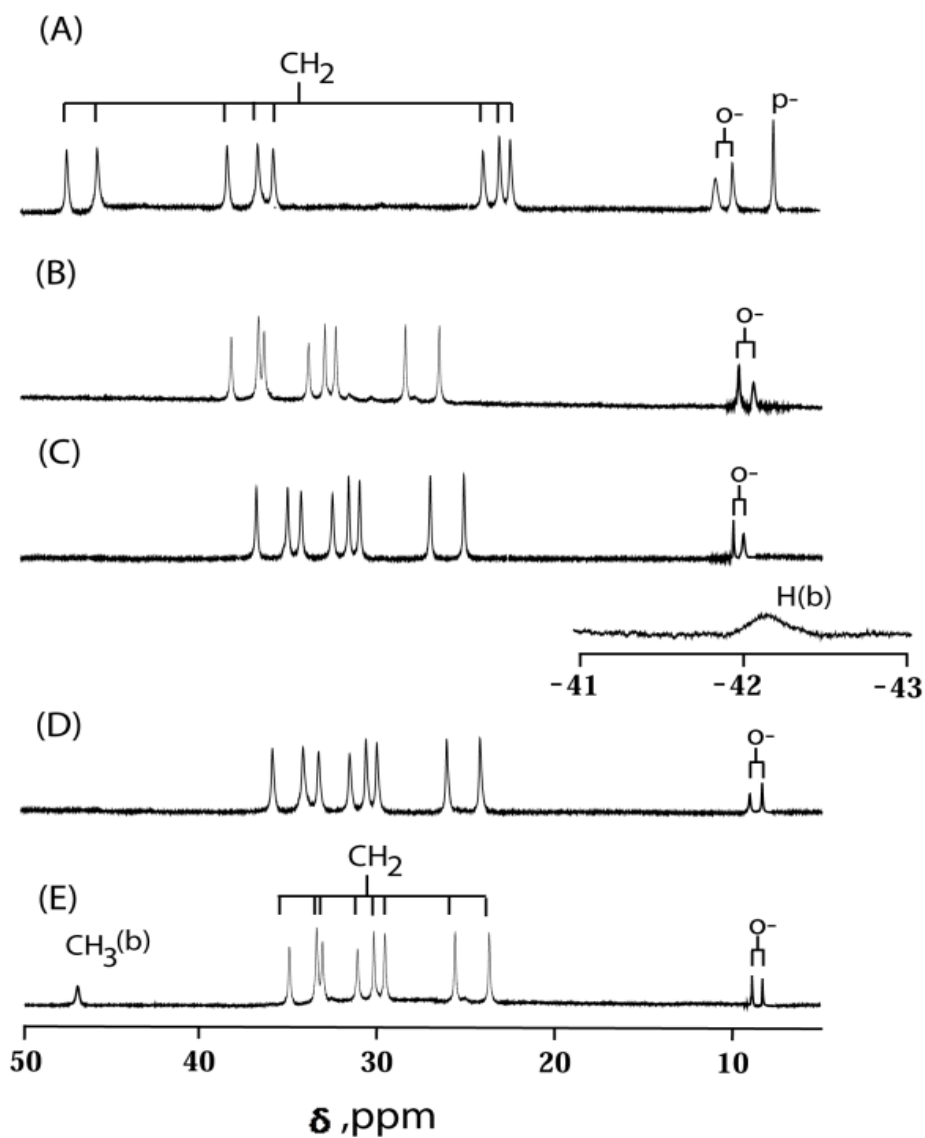
A family of binuclear highly substituted and distorted ferric porphyrins bridged through a variety of  $p$ -hydroquinone dianion has been reported here. Iron centres are involved in weak antiferromagnetic exchange interactions, the extent of which depends on the electronic nature of the bridge.



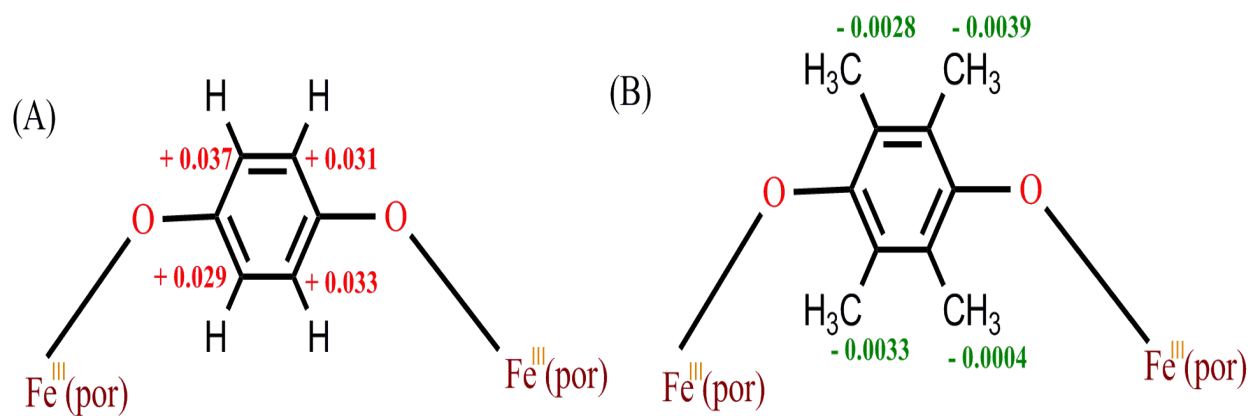
$R_1$	$R_2$	$R_3$	$X$	$Y$	Complex
Me	H	Me	Cl	Cl	<b>2a</b>
OMe	OMe	OMe	CN	Cl	<b>2b</b>
OMe	OMe	OMe	Cl	Cl	<b>2c</b>
OMe	OMe	OMe	H	H	<b>2d</b>
OMe	OMe	OMe	Me	Me	<b>2e</b>



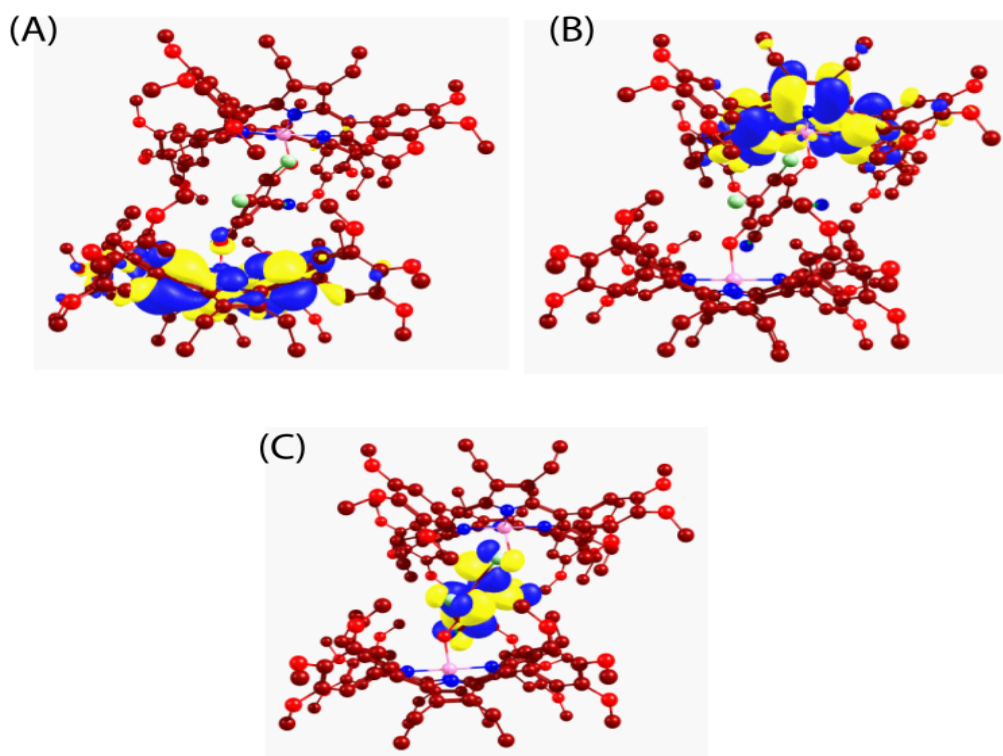
**Figure.**  $\chi_M T$  versus  $T$  plots of the crystalline samples of **2b** (o), **2c** ( $\Delta$ ), **2d** ( $\square$ ) and **2e** ( $\square$ ). The solid lines are the best fits using the values given in the text. Plot of the  $pK_a$  of the *p*-benzoquinone versus the coupling constant ( $J$ ) of the complexes. The  $pK_a$  values are: 2,3,5,6-tetramethyl-1,4-benzoquinone (DuQ): 11.5, 1,4-benzoquinone (Q): 11.4, 2,3,5,6-tetrachloro-1,4-benzoquinone (ClQ): 8.4, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ): 3.4



**Figure 1.**  $^1\text{H}$  NMR (at 295 K in  $\text{CDCl}_3$ ) spectra of (A) **2a**, (B) **2b**, (C) **2c**, (D) **2d**, and (E) **2e**.



**Figure 2.** Mulliken spin densities of bridging carbon atom calculated for (A) **2d**, and (B) **2e**.



**Figure .** (A) HOMO, (B) LUMO and (C)  $\alpha$ -HOMO-4 of complex **2b** calculated by using DFT. The contour values are  $\pm 0.02$  au for the complex.

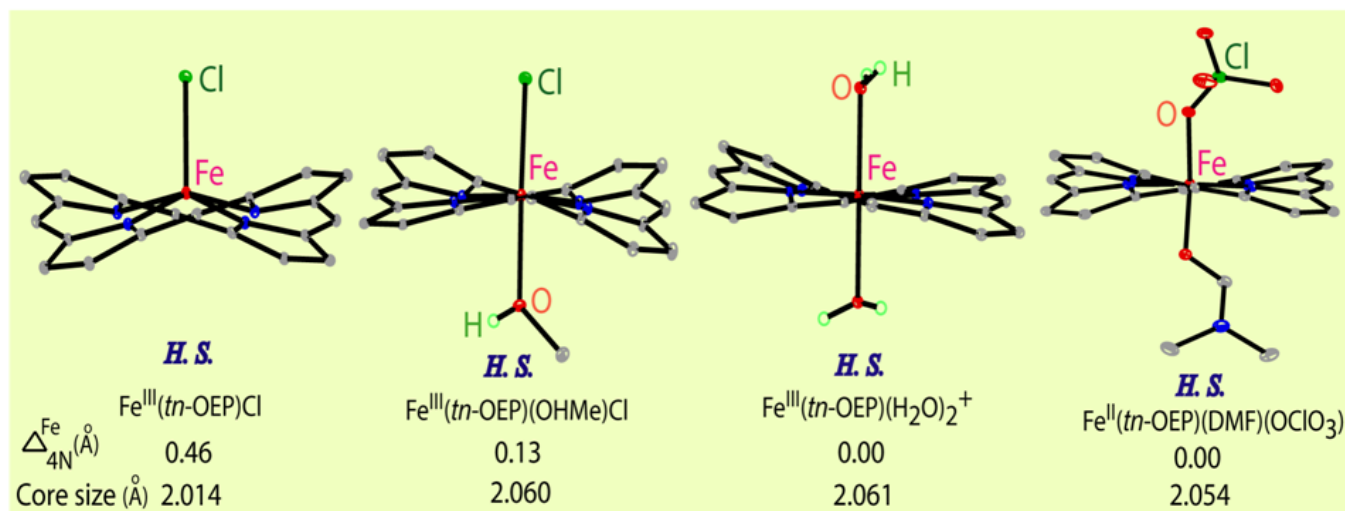
### ❖ Metal-ion Displacement and Axial Ligand Orientation:

Hemoproteins serve many diverse biological functions through the nearly identical heme prosthetic group that displays a range of distorted nonplanar shapes. The importance of nonplanar heme structures in a variety of proteins is amplified by the observation that heme is nonplanar inside the protein environment but almost planar outside. It is believed that conformational control of the chromophore by the protein side chains can account for the various functions of chemically similar tetrapyrrole pigments found in nature and thus become an attractive subject to investigate the relationship between the macrocycle distortion and the properties of the metal center in porphyrin complexes. Knowledge of these interrelationships will certainly help to sort out the essential parameters that govern the specific action of the hemoproteins in biological processes. The nature and extent of non-planarity in heme was successfully demonstrated to be instrumental in modulating the metal ion displacement from porphyrin mean plane, axial ligand orientations, metal spin and redox properties and even axial ligand affinity which enable isolation

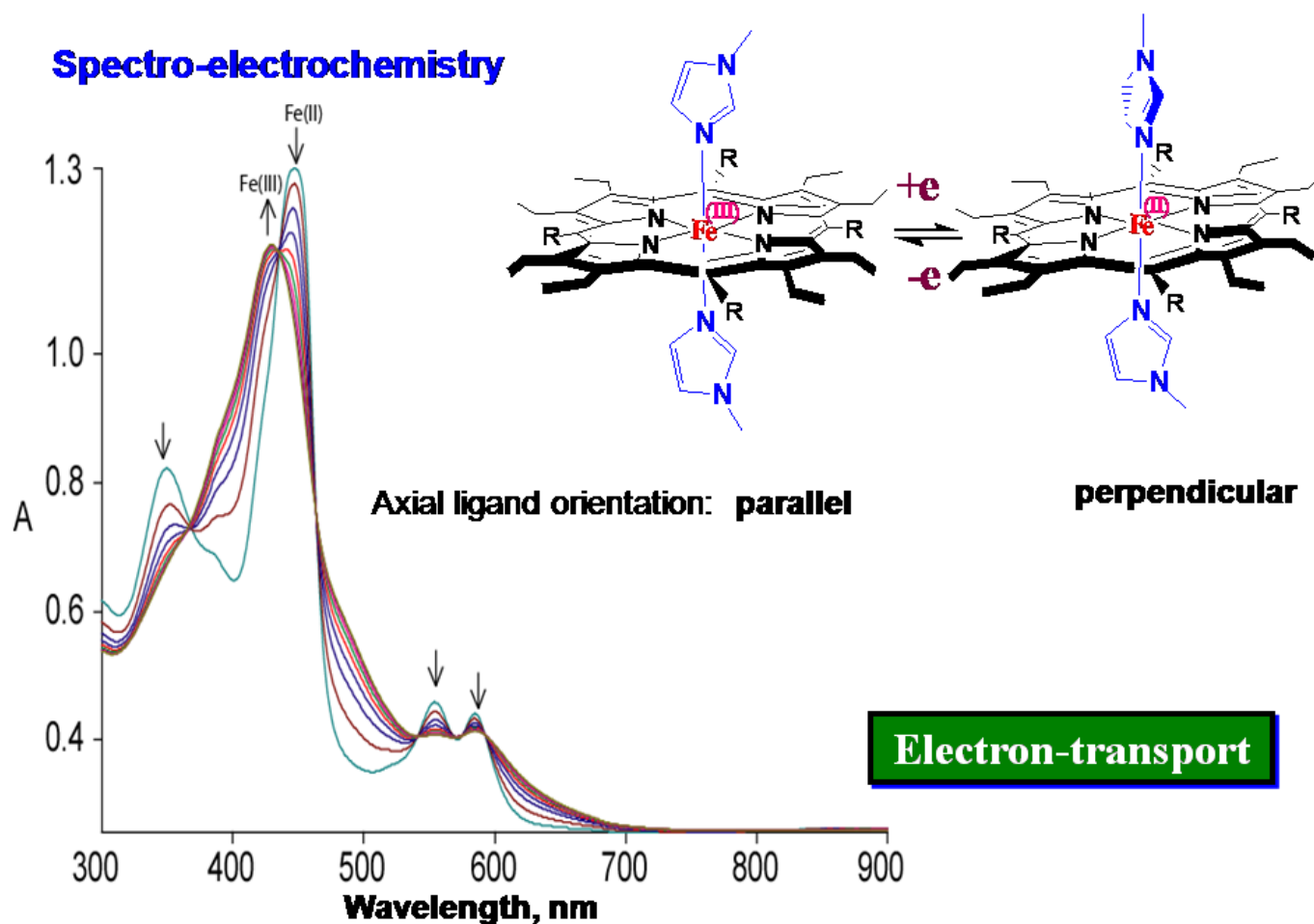


in the solid state of a hitherto unknown family of highly distorted six-coordinated vanadyl porphyrins incorporating axial ligand L (L: pyridine, THF and MeOH), for the first time.

## ❖ Metal ion displacement in non-planar heme environment



## Axial Ligand Orientation: In Non-planar Environment





## Representative Publications:

- 1. Hydrogen-Bonding Interactions Trigger a Spin-Flip in Iron(III)-Porphyrin Complexes**  
D. Sahoo, M. G. Quesne, S. P. de Visser\* and S. P. Rath\*  
*Angew. Chem. Int. Ed.* **2015**, *54*, 4796 - 4800.
- 2. Controlled Generation of Highly Saddled (porphyrinato) Iron(III) Iodide, Tri-iodide and One-electron Oxidized Complex**  
D. Sahoo, and S. P. Rath\*  
*Chem. Commun.* **2015**, *51*, 16790-16793.
- 3. Binuclear Highly distorted Iron(III) Porphyrins Bridged by the Dianions of Hydroquinones: Role of Bridge in the Electronic Communication**  
D. Sahoo, A. K. Singh and S. P. Rath\*  
*Eur. J. Inorg. Chem.* **2016**, 3305-3313.
- 4. Spin Modulation in Highly Distorted Fe(III) Porphyrinates Using Axial Coordination and their  $\pi$ -Cation Radicals**  
D. Sahoo, T. Guchhait and S. P. Rath\*  
*Eur. J. Inorg. Chem.* **2016**, 3441-3453.
- 5. Building-up Remarkably Stable Magnesium Porphyrin Nano-Structures in One Pot: Synthesis, Structure, Surface Morphology and Effect of Bridging Ligands**  
Sk A. Iqbal, S. Brahma and S. P. Rath\*  
*Inorg. Chem.* **2012**, *51*, 9666 - 9676.
- 6. Switching Orientation of Two Axial Imidazole Ligands between Parallel and Perpendicular in Low-Spin Fe(III) and Fe(II) Nonplanar Porphyrinates**  
R. Patra, D. Sahoo, S. Dey and S. P. Rath\*  
*Inorg. Chem.* **2012**, *51*, 11294 - 11305.

7. **Effects of Axial Pyridine Coordination in a Saddle-Distorted Porphyrin macrocycle: Stabilization of Hexa-coordinated High-Spin Fe(III) and Air-stable Low-Spin Iron(II) Porphyrinates**  
R. Patra, S. Bhowmik, S. K. Ghosh and S. P. Rath\*  
*Dalton Trans.* **2010**, 39, 5795 - 5806.
8. **Axial Ligand Orientations in a Distorted Porphyrin Macrocycle: Synthesis, Structure and Properties of Low-Spin bis (Imidazole) Fe(III) and Fe(II) porphyrinates**  
R. Patra, A. Chaudhary, S. K. Ghosh and S. P. Rath\*  
*Inorg. Chem.* **2010**, 49, 2057 - 2067.
9. **Cyanide Binding to Iron in a Highly Distorted Porphyrin Macrocycle: Synthesis and Structure of Low-spin Fe(II) dicyano Porphyrin**  
R. Patra and S. P. Rath\*  
*Inorg. Chem. Commun.* **2009**, 515 - 519.
10. **Modulation of Metal Displacement in a Saddle Distorted Macrocycle: Synthesis, Structure, and Properties of High Spin Fe(III) porphyrins and Implications for the Hemoproteins**  
R. Patra, A. Chaudhary, S. K. Ghosh and S. P. Rath\*  
*Inorg. Chem.* **2008**, 47, 8324 - 8335.
11. **Axial Ligand Coordination in Sterically Strained Vanadyl Porphyrins: Synthesis, Structure, and Properties**  
S. K. Ghosh, R. Patra and S. P. Rath\*  
*Inorg. Chem.* **2008**, 47, 9848 - 9856.