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Conversion of Electron Configuration of Iron Ion through Core Contraction of Porphyrin: Implications for Heme Distortion

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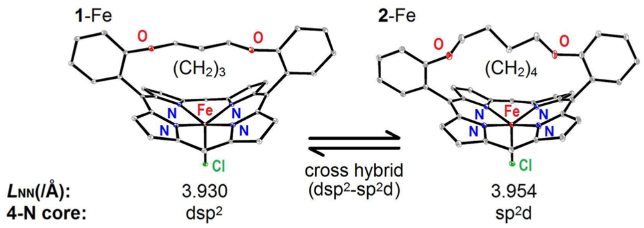
ABSTRACT



It was demonstrated experimentally that nonplanar iron porphyrins can be induced to undergo a conversion in their electronic configuration to form a cross-hybrid transition by compressing the macrocyclic core size for the central metal ion. A series of monostrapped iron porphyrins were used as model systems, and their electronic properties were probed using electron spin resonance and differential spectral analyses. These results indicate that the formation of a cross-hybrid transition stage is related to the stability of the high-valence state and potent oxidizing ability of the central iron ion.

For some time, it was generally believed that the functions of the heme depended on the peripheral environment of the macrocycle,[1,2] and very little attention was given to the impact of changes in the macrocycle itself. Recent studies, however, have suggested that conformational changes in the heme macrocycle may play a more important role in heme function than that of the surrounding environment.[3,4] The nonplanarity of heme has been recognized as a structural feature that is conserved in specific proteins.[5] The potent oxidizing ability of heme is capable of hydroxylating inactivated C−H bonds.[6] The nonplanarity of porphyrins has received considerable attention because of its significance in proteins,[7] and nonplanar porphyrins also exhibit a significant number of specific properties including catalytic ability,[8] tunable axial binding,[9] and significant spectral red shifts.[10] Distortions of this type are energetically unfavorable, suggesting that they are crucial to the functions of heme and porphyrins.[11]

In our more recent report,[12] we clarified the role of the macrocyclic deformation modes and distortion degree in heme for a series of ruffle-type 5,15-10,20-distrapped free-base porphyrins and a dome-type capped porphyrin. The results indicated that the free 4-N core in these two types of

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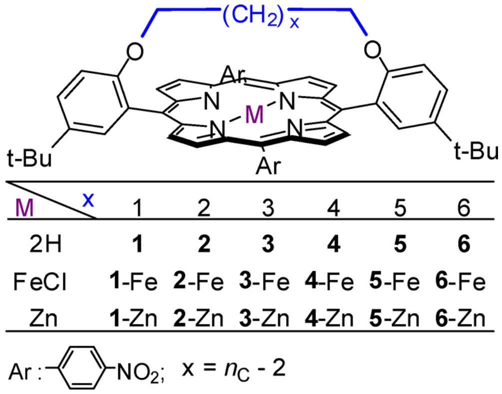
nonplanar systems exhibited an opposing trend as the degree of distortion increased, in that they took on a larger size range than the free diameter of the iron ion.[13]

These findings provided some theoretical understanding as to how distorted heme can stabilize the unligated Fe(II) oxidation state[14] and also generate the high-valent iron(V)-oxo complex[15] by changing its deformation modes and adjusting its distortion degree. Unfortunately, however, these synthetic distrapped-type porphyrins cannot be metalized under the existing conditions because the two straps block this process, and changes to the electronic properties of the central metal following core contraction can therefore not be explored experimentally.[12]

Scheme 1. Model Compounds: Free-Base Porphyrins **1**–**6**, Their Iron **1**-Fe to **6**-Fe and Zinc Complexes **1**-Zn to **6**-Zn

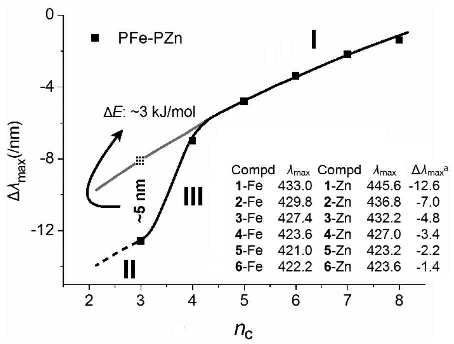


M \ x	1	2	3	4	5	6
2H	**1**	**2**	**3**	**4**	**5**	**6**
FeCl	**1**-Fe	**2**-Fe	**3**-Fe	**4**-Fe	**5**-Fe	**6**-Fe
Zn	**1**-Zn	**2**-Zn	**3**-Zn	**4**-Zn	**5**-Zn	**6**-Zn

Ar : $-C_6H_4-NO_2$; $x = n_C - 2$

We developed an interest in what would happen if the core size became less than the minimum value of the central free metal ions. The macrocyclic distortion and resulting core contraction can result in changes in the electronic and magnetic properties of the central iron ion[16] and a spectral shift for the porphyrin ring.[17,18] Three series of monostrapped nonplanar porphyrins[10] in their free-base forms **1**–**6**, their iron complexes **1**-Fe to **6**-Fe, and their zinc complexes **1**-Zn to **6**-Zn (Scheme 1) were selected as replaceable model systems of the ruffle-type porphyrins for the above target.

In the current report, we have demonstrated experimentally that nonplanar iron porphyrins can be induced to generate a conversion in the electronic configuration and form a cross-hybrid transition of the central metal ion by compressing the 4-N core in size. The electronic properties of six monostrapped iron porphyrins have been probed using the differential spectra and electron spin resonance (ESR) method. A radical occurred when a 4-N electron pair partially occupied the $3d_{z^2}$ orbital of the central iron ion, leading to the formation of a cross-hybrid transition. These findings revealed that the occurrence of the transition stage was related to the stability of the high-valence state and potent oxidizing ability of the central iron ion.



Compd	λ_{max}	Compd	λ_{max}	$\Delta\lambda_{max}$[a]
1-Fe	433.0	**1**-Zn	445.6	-12.6
2-Fe	429.8	**2**-Zn	436.8	-7.0
3-Fe	427.4	**3**-Zn	432.2	-4.8
4-Fe	423.6	**4**-Zn	427.0	-3.4
5-Fe	421.0	**5**-Zn	423.2	-2.2
6-Fe	422.2	**6**-Zn	423.6	-1.4

Figure 1. Differential spectra of the strapped iron porphyrins **1**-Fe to **6**-Fe to the corresponding zinc complexes **1**-Zn to **6**-Zn at the Soret band in a $CHCl_3$ solution ($\sim 2.0 \times 10^{-6}$ M) at 293 K. [a]$\Delta\lambda_{max}$ is the spectral shift of the maxima between each iron porphyrin (e.g., **1**-Fe) and its corresponding zinc one (**1**-Zn). The dotted line represents the predicted trend.

The differential spectra obtained from a comparison of the iron and zinc porphyrins can systematically deduct their spectral shift from size difference of metals.[19] The conversion process was reflected in their absorptive spectra.[20] The spectral shift of a distorted porphyrin provides a means of following changes in the ground energy level.[10] For the iron porphyrins, **1**-Fe to **6**-Fe, the spectral shifts did not exhibit a continuous trend and present an inflection point at $n_C = 4$.

The differential value, $\Delta\lambda_{max}$, represents the spectral shift between the iron porphyrin and the corresponding zinc porphyrin (Figure 1). For compounds **2**-Fe to **6**-Fe, the electronic spectra showed a regular red shift under a low degree of distortion ($n_C > 4$), whereas compound **1**-Fe exhibited a ~5 nm deviation from the extended trend line based on the curve for compounds **2**-Fe to **6**-Fe. This deviation indicated an increase of ~3 kJ/mol for the energy level. Inspection of the graph revealed that the line can also be divided into three sections (I, II, and III).

The crystal structures of the model compounds revealed that their macrocycles adopted a ruffle-like deformation due to the shrinkage caused by the straps, and the core size became smaller as the straps were shortened. Furthermore, the cavity diameter of compound **1**-Fe was 3.930 Å and

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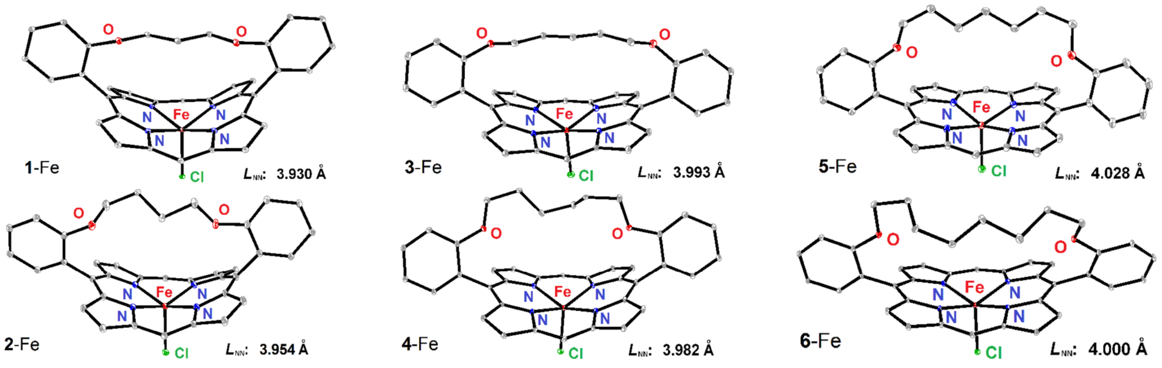

Figure 2. Crystal structures of compounds **1**-Fe to **6**-Fe (strap is from $(CH_2)_3$ to $(CH_2)_8$). The symbol, L_{NN}, is the averaged length between the diagonal N atoms in the porphyrin center. The substituents, *tert*-butyl group, and peripheral protons have been omitted for clarity.

therefore less than the minimum value of free diameter (L_{NN} = 3.94 Å) of a iron ion.[13] The cavity parameters for the six compounds, **1**-Fe to **6**-Fe, are shown in Figure 2.

An early report demonstrated that the porphyrin core can be expanded or contracted by regulating the spin state of the nickel(II) ion within the porphyrin.[21,22] It remained unclear, however, whether the electronic spin state of the metal ion could, in turn, be converted during the contraction of the core. For the iron(III) porphyrins **1**-Fe to **6**-Fe, the core size tended to increase as the n_C value increased, as evidenced by a plot of L_{NN} against n_C (Figure 3). The size contraction appeared as two independent trends depending on whether there was an odd or even number of carbon atoms in the strap. The core size of compound **1**-Fe (3.930 Å) appeared as a clear deviation (~0.02 Å) from the trend line derived from the two curves. A transition stage occurred between **1**-Fe and **2**-Fe, outlining a change in the trend (black line), which also implied that that a core size value of ~3.95 Å represented a critical size in the conversion of the electron configuration of the iron ion. The black trend line was subsequently divided into three separate stages that corresponded to the outer (I), inner (II), and cross-hybrid stages (III), which was completely consistent with three stages encountered during the differential spectra (Figure 1).

Any conversion in the electronic configuration in this context inevitably leads to a change in some of the spectral properties.[16,23] Further information relating to the impact of the core size on the conversion of the electronic configuration and formation of a cross-hybrid transition was obtained from the ESR results. ESR measurements for the toluene solution of **1**-Fe to **6**-Fe were performed in inert gas at 130 K, effectively avoiding intermolecular electron exchange interactions.

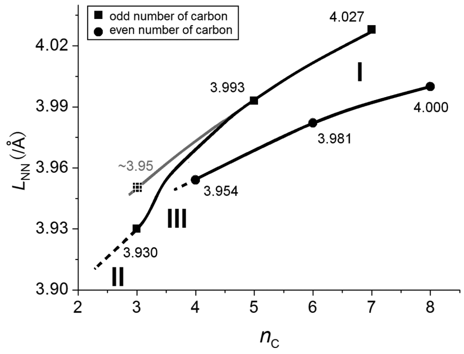

Figure 3. Relationship of the core size (L_{NN}) to the number of carbon atoms (n_C) in the straps according to the crystal structures of compounds **1**-Fe to **6**-Fe in Figure 2. The dotted line represents the predicted trend.

The ESR results for the six current compounds indicated that the conversion of the electronic configuration occurred, resulting in the formation of a cross-hybrid transition in the central metal ion (Figure 4). A possible electron exchange between the outer $4d_{xy}$ orbital and the inner $3d_z{}^2$ one will take place under full core contraction; that is, a lone pair electrons occupied in the $4d_{xy}$ orbital is transferred to the $3d_z{}^2$ one, and the original unpaired electron in the $3d_z{}^2$ orbital is repelled to either localize in the $4d_{xy}$ one or delocalize in the conjugation macrocycle. A marked radical signal (* in Figure 4) was obtained for compound **1**-Fe and can be attributed to the delocalization of the unpaired electron. It was thought that the 4-N unit effectively maintained the outer sp^2**d** hybrid mode in compounds **3**-Fe to **6**-Fe and completely changed to the inner **d**sp^2 form in compound **1**-Fe. A new signal (g = 2.2), however, was observed exclusively in compound **1**-Fe, which can be attributed to the repulsion of the 4-N electron pair to the 3d electron resulting in the formation of a metastable state. For compound **2**-Fe, it can be thought that the 4-N unit existed in a mixed sp^2**d**↔**d**sp^2 form.

The ESR spectra of all of the samples contained the high-spin (HS) Fe(III) (S = 5/2) feature (marked

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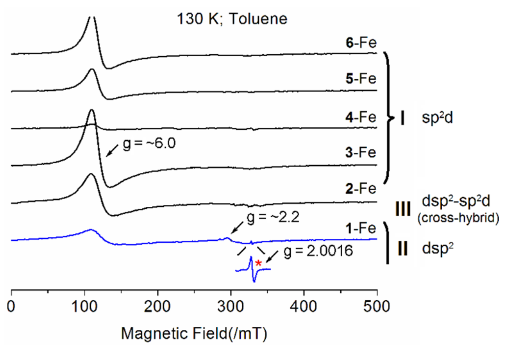

Figure 4. ESR spectra of the single crystal of iron porphyrins **1**-Fe to **6**-Fe and the central metallic hybrid mode. The insets represent the determined temperature and solvent, and the red symbol (*) denotes the radical.

by $g = \sim 6.0$).[16,24,25] The signal ($g = 6.0$) for compound **1**-Fe was derived from the complete transfer of the 4-N electron pair to a $3d_{z^2}$ orbital and the formation of a new Fe(III) spin state, which was different from those for the other five compounds. The formation of a radical provided evidence for the formation of an active electron under the core contraction conditions and the occurrence of Compound I, a cation radical, in the heme cycle during macrocyclic deformation,[15,26] which guarantees the potent oxidizing ability of the central iron ion. The ESR results effectively consolidated these results when they were determined from the solid or from a solution at room temperature (see Supporting Information S9–S13).

A larger $\Delta\lambda_{max}$ value was related to a larger change in the ground energy level (ΔE). These spectral shifts and changes in the energy level indicated that the conversion of configuration required the macrocycle to possess a suitable 4-N cavity and that the formation of the cross-hybrid transition needed a much lower energy than that of the inner **d**sp^2 state (Figure 1).

The formation of such a transition stage and the stability of the high-valence central iron ions were also assessed using DFT calculations.[27] The measured Fe(IV)–N bond length[13] was smaller than that of a lower valence Fe(III)–N bond. The computational results revealed that there was an L_{NN} difference of 0.08 Å between the Fe(III) and Fe(IV) porphyrins with the same strap size (see Supporting Information). This difference was relative to the deviation observed in the crystal results, although the value is much larger (Figure 3). Both of the ions possessed the d^5 and d^4 configurations, and their 4-N unit would consequently adopt an outer sp^2**d** and inner **d**sp^2 hybrid mode. The higher valence ion (e.g., Fe(IV)) required a smaller 4-N cavity that could, in turn, stabilize the higher valence iron ion Fe(IV).

Note that the deviation in the central metal ion from the 4-N plane could effectively offset any increase in the electron cloud density in these ruffle-like strapped compounds, which would be apt to maintain the Fe(III) valence throughout the core contraction. While the occurrence of a deviation would be difficult in the ruffle or saddle porphyrins, the dominant deformations in heme, because of the equivalent features in two sides of the macrocycle, would effectively drive the removal of an electron to produce a higher valence, Fe(IV).

Macrocyclic deformation of porphyrins is a nonspontaneous process, in that the formation of a cross-hybrid transition is energetically unfavorable. This is the critical difference between the current discussion and existing organometallic theories.[28,29] For example, the formation of a cross-spin state[28] can provide low-energy pathways for otherwise difficult processes because of spin-crossing effects. The formation of a cross-hybrid transition therefore requires a special deformation structure (e.g., the macrocyclic distortion of a porphyrin), whereas the cross-spin state can form in common organometallic systems.

In conclusion, iron porphyrins can be induced to change their 3d electronic configuration and form a cross-hybrid transition by contracting their core size. The significance of the transition stage lies in the observation that a repelled 3d electron (as a radical) tends to leave and a stable high-valent iron material is formed when the core contracts; the electron will return to its original 3d orbital, and the central ion maintains the low-valent state if the core recovers in size. Our findings provide an insight into the unique biochemical functions of heme and also add to our current understanding of theories in bioinorganic chemistry.

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Supporting Information Available. Crystal structures, experimental procedures, and characterization of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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