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Ruffling Deformations of Nickel(II) and Zinc(II) Hydroporphyrin and Chlorophin Complexes: Implications for F₄₃₀, the Nickel Tetrapyrrole Cofactor of Methylcoenzyme M Reductase[†]

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Nonlocal DFT provides an excellent description of the structural and conformational properties of metallohydroporphyrins and related complexes. The Ni(II) complexes are found to be strongly ruffled and the Zn(II) complexes planar, consistent with experimental results. The increased flexibility of the novel chlorophin, bacteriophin, and isobacteriophin ligands, relative to hydroporphyrins, appears to result from a widening of the C_α–N–C_α angle at the imine nitrogen. A key finding relevant to understanding the chemistry of cofactor F₄₃₀ is that seemingly innocent substituents such as methyl and phenyl groups can exert a dramatic impact on the metal coordination geometry and macrocycle conformation of Ni(II) hydroporphyrins and related complexes, shrinking Ni–N bond distances and leading to significantly greater ruffling.

Introduction

Nonplanar porphyrins and related macrocycles are ubiquitous as synthetic substances and as cofactors in protein environments.¹ Indeed, specific types of macrocycle nonplanarity appear to be conserved features of a number of classes of heme proteins.¹ Thus, much attention has focused in recent years on the electronic–structural consequences and possible biological significance of nonplanar distortions of porphyrins and related macrocycles. Until now, molecular mechanics (MM) calculations have been the major computational tool for studying nonplanar porphyrins.¹ However, MM is not readily applicable to molecules with unusual electronic structures such as those containing transition metal centers in unusually high or low oxidation states. High-quality quantum chemical methods, generally much more computationally demanding than MM, have a major advantage in this regard in that they can provide a complete package of information encompassing both geometrical and electronic–structural aspects of the molecules studied. Among the different quantum chemical methods available for studying nonplanar transition metal porphyrins, density functional theory (DFT) appears to be uniquely suitable, both for its computational expediency compared to traditional *ab initio* correlated methods and for the accuracy of the calculated molecular properties.² Recently, we have used DFT to accomplish a fairly comprehensive analysis of the factors controlling ruffling distortions of porphyrins.³ Here we present a DFT treatment of another facet of nonplanar distortions of porphyrins and related molecules, viz., a study of ruffling distortions of hydroporphyrins and related ring systems as a function of metal ion size. Figure 1 defines the ruffling torsion angle, which is denoted as ρ in Figures 2–4.

A major long-term goal of our studies on nickel porphyrinoids is to obtain a quantum chemical description of the unique chemistry of cofactor F₄₃₀,⁴ a nickel tetrapyrrole cofactor of methylcoenzyme M reductase, the enzyme that catalyzes the final stages of the reduction of carbon dioxide to methane in

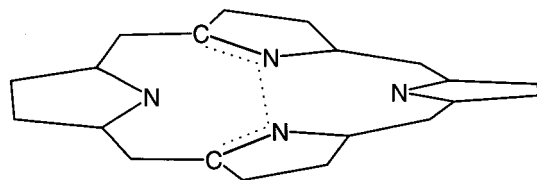


Figure 1. Definition of the C_α–N–N–C_α ruffling torsion angle.

methanogenic bacteria. As a first step toward achieving this goal, we simply aimed at validating the performance of nonlocal DFT in describing the conformational characteristics of metallohydroporphyrins as a function of the size of the coordinated metal ion. This modest goal was fulfilled: nonlocal DFT is indeed a suitable method for this type of calculations. Gratifyingly, the results proved to be of considerable chemical interest as well, providing a deeper understanding of some of the factors controlling ruffling deformations in metallohydroporphyrins, as mentioned below.

Dolphin and co-workers have recently reported X-ray crystallographic characterization of some nickel chlorophin complexes.⁵ In particular, they comment on the “astonishing” degree of ruffling of the sterically unencumbered nickel(II) *meso*-tetraphenylchlorophin. Intrigued by this observation, we have studied here nickel(II) and zinc(II) complexes of chlorophin, bacteriophin, and isobacteriophin ligands.⁶ The results provide additional insights into the conformational preferences of these lesser known ligands.

Piqued by certain significant disagreements between the optimized geometries of unsubstituted metallohydroporphyrins and the crystallographic structures of relevant peripherally substituted compounds, we carried out geometry optimizations of the nickel(II) complexes of *meso*-tetramethylisobacteriochlorin⁷ (TMI) and *meso*-tetraphenylchlorophin (TPCph),⁵ two peripherally substituted molecules that have been crystallographically analyzed. The results show that seemingly innocent peripheral substituents may be responsible for striking changes in the coordination geometry of the nickel center as well as in macrocycle con-

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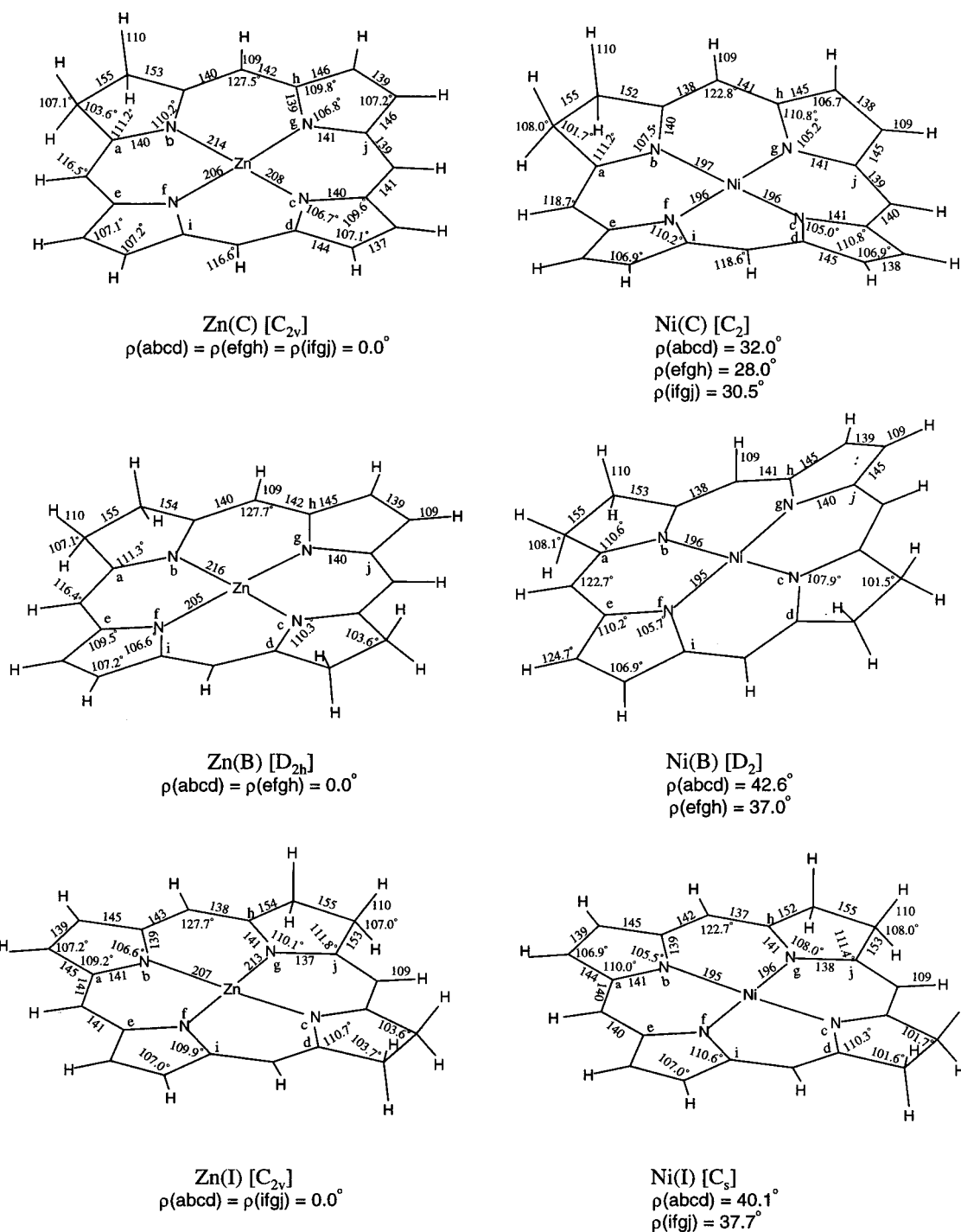


Figure 2. Optimized geometries (pm, deg) of metallohydroporphyrins.

formation, a finding of considerable relevance to the theoretical modeling of F_{430} , which has an elaborate and complex substitution pattern.

Methods. The calculations described herein were generally carried out using the Gaussian 98 program system.⁸ We used the PW91 functional, the medium-sized LANL2DZ basis set, and tight criteria for geometry optimizations. In unpublished work on models of peroxidase compounds I and II, we have found that PW91/LANL2DZ calculations provide a good description of the molecular geometries and vibrational frequencies of a number of different transition metal porphyrins. Figure 2 shows the optimized geometries of the metallohydroporphyrins. Figure 3 shows the optimized geometries of metallochlorophyllin and related complexes. Figure 4 shows the optimized geometries

of Ni(TMI) and Ni(TPCph). The molecular point groups shown in Figures 2–3 describe the unconstrained optimized structures and do not refer to constraints on the optimizations. In addition, we also optimized Ni(TMI) with a Slater-type triple- ζ plus polarization (TZP) basis set (and the PW91 functional and the ADF⁹ program system) to confirm that the PW91/LANL2DZ geometries are indeed converged with respect to improvement of the basis set.

Results and Discussion

(a) Metallohydroporphyrins. Figure 2 shows that Ni(C) is ruffled with ruffling torsion angles ranging from 28 to 32°. Ni(B) and Ni(I) are even more ruffled with ruffling torsion angles

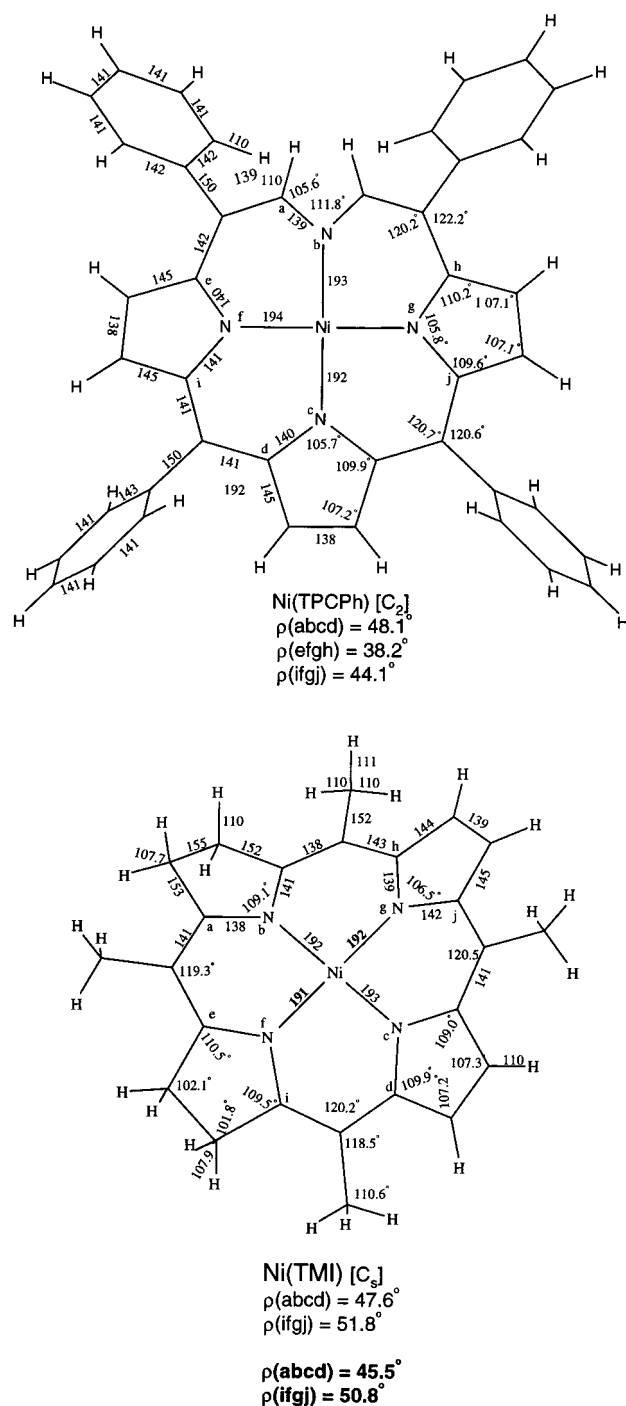


Figure 4. Optimized geometries (pm, deg) of Ni(TPCph) and Ni(TMI). For Ni(TMI) the numbers in bold refer to PW91/TZP results.

hydroporphyrin complexes and, thus, by themselves, do not furnish any insight into the greater flexibility of chlorophin-type ligands relative to hydroporphyrins.

For the zinc complexes, there are two very different groups of Zn–N distances, the Zn–N distances involving the “imine” nitrogens being particularly long at 217–222 pm, significantly longer than analogous distances in Zn(II) hydroporphyrins. As in the case of metallohydroporphyrins, the Ni(II) complexes are severely ruffled while the Zn(II) complexes are planar. We conclude from this that the “imine” nitrogen does have a general tendency to form long metal–nitrogen bonds, but the low-spin Ni(II) ion, which forms particularly strong metal–ligand σ bonds by virtue of its “empty” $d_{x^2-y^2}$ orbital, appears to exert a leveling effect on metal–nitrogen bond distances.

Finally, the $C_\alpha-N-C_\alpha$ angles in metallochlorophin and related complexes are significantly wider than those in the reduced rings of analogous metallohydroporphyrin complexes. Ruffling distortions in metalloporphyrins correlate well with widening $C_\alpha-N-C_\alpha$ angles.^{2,12} This, then, appears to be the key factor contributing the “increased flexibility of the degraded porphyrin framework”.⁵

(c) Substituent Effects on Coordination Geometry and Macrocycle Conformation. The optimized structural data shown in Figures 2 and 3 on one hand and crystallographic data on relevant experimentally studied molecules on the other hand appear to disagree in a key respect: the optimized Ni–N bond distances of 195–197 pm in Figures 2 and 3 are significantly longer than experimentally determined Ni–N distances in ruffled porphyrin- or hydroporphyrin-type complexes, which hover around 190 pm. A discrepancy of this magnitude can seriously detract from the credibility and potential usefulness of DFT optimizations of novel Ni(II) tetraazamacrocycles. We suspected that peripheral substituents, present in all crystallographically studied molecules but ignored in our calculations, may account for part of this discrepancy, a surmise that proved to be correct. The optimized molecular structures of Ni(TPCph) and Ni(TMI) shown in Figure 3 indeed exhibit considerably shorter Ni–N distances of 1.92–1.94 Å and higher ruffling torsion angles than the unsubstituted molecules, Ni(Cph) and Ni(I). The two molecules Ni(TPCph)⁵ and Ni(TMI)⁷ have also been characterized crystallographically, and the crystallographic and optimized geometries are generally in excellent agreement. As hoped for, the PW91/TZP optimization of Ni(TMI) gave slightly shorter Ni–N distances of 1.91–1.92 Å, in essentially perfect agreement with experiment.⁷ These results demonstrate that seemingly innocent peripheral substituents such as methyl and phenyl groups can dramatically affect the metal coordination geometry and macrocycle conformation.¹³

At the cost of digressing somewhat, a brief comment is in order on the optimized PW91/TZP Ni–N bond distances of 1.96 Å obtained for the Ni(III) complex, [Ni^{III}(P)(Py)₂]⁺ (*D*_{2d}; P = unsubstituted porphyrin, Py = pyridine).¹⁴ At first sight, these bond distances may appear to be unreasonably high, not only in view of the +III oxidation state of the metal but also because the optimized structure features a fairly strongly ruffled porphyrin macrocycle with a ruffling torsion angle of 37°. However, the above results on Ni(TPCph) and Ni(TMI) suggest that geometry optimization of a substituted complex such as [Ni^{III}-(TPP)(Py)₂]⁺ (TPP = *meso*-tetraphenylporphyrin) would lead to significantly shorter Ni^{III}–N bond distances, a speculative remark that we hope to confirm.

(d) Implications for F₄₃₀. The results described above in section (c) made us more aware of the subtle but extremely important role played by the complex substitution pattern of F₄₃₀ (Figure 5) in controlling its unique chemistry.⁴ The isolated cofactor F₄₃₀ is thermodynamically unstable relative to its 12-, 13-diepimer and isomerizes to the latter over time. However, only the native stereoisomer stabilizes Ni(I), the so-called active red1 state of methylcoenzyme M reductase. Native four-coordinate Ni(II) F₄₃₀ also has a dramatically higher axial ligand affinity relative to its diepimer. At the time of original submission of this paper, the results described above promised to serve as a prelude to a more complex project aimed at understanding and modeling the interplay of skeletal stereo-isomerism and the unusual transition metal chemistry exhibited by coenzyme F₄₃₀. Gratifyingly, at the time this paper is being revised and resubmitted, this promise has largely come to fruition and some results on “high-fidelity” models of coenzyme

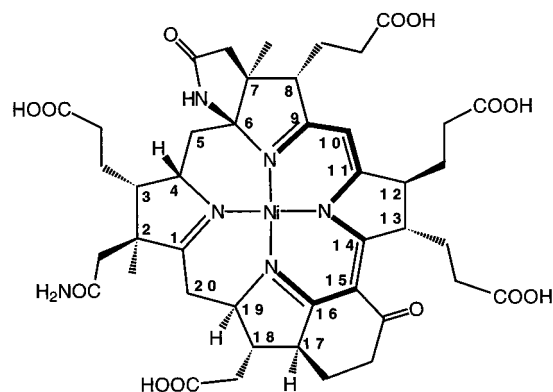


Figure 5. Coenzyme F_{430} , with standard numbering of its tetrapyrrole skeleton.

F_{430} have been published.¹⁵ Some key conclusions from that work, repeated below, should assist in placing the results obtained here in their biochemical context.

Although the unique chemistry of F_{430} has inspired a vast body of fundamental research on nonplanar porphyrins and hydroporphyrins, our DFT modeling studies¹⁵ on F_{430} suggested that, ironically, it is precisely its relative inability to undergo strong ruffling, as a result of steric constraints imposed by its peripheral substituents, that dictates its unique chemistry, including its ability to stabilize Ni(I). We concluded that the molecular architecture of F_{430} appears to be designed for occupancy of the Ni $d_{x^2-y^2}$ orbital. Ongoing studies in our laboratory suggest that this may also explain the possible stabilization by F_{430} of formally Ni(III)– CH_3 intermediates with the unusual $d_{xy}^2 d_{xz}^2 d_{yz}^2 d_{x^2-y^2}^1$ d-electron configuration.¹⁵

Conclusion

Nonlocal DFT appears to provide an excellent description of the structural and conformational properties of metallohydroporphyrins and related complexes. In general, the Ni(II) complexes are strongly ruffled and the Zn(II) complexes have planar equilibrium geometries. The calculations afford certain fresh insights into the structural chemistry of this class of complexes.

The increased flexibility of chlorophin and related ligands, relative to hydroporphyrins, results primarily from a widening of the $C_\alpha-N-C_\alpha$ angle at the imine nitrogen.

Seemingly innocent substituents such as methyl and phenyl groups exert a dramatic impact on the metal coordination geometry and macrocycle conformation of Ni(II) hydroporphyrins and related complexes, a finding clearly relevant to

understanding the chemistry of cofactor F_{430} , which has a relatively complex substitution pattern.

Finally and somewhat ironically, we have shown elsewhere¹⁵ that coenzyme F_{430} , which has inspired many studies on nonplanar porphyrins and hydroporphyrins, is an atypical hydroporphyrin: the particular stereochemistry of its substituents discourages strong ruffling, and this relative flatness is the basis for its unique stabilization of Ni(I).

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