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Fixation of Zinc(II) Ion to Dioxygen in a Highly Deformed Porphyrin: Implications for the Oxygen Carrier Mechanism of Distorted Heme

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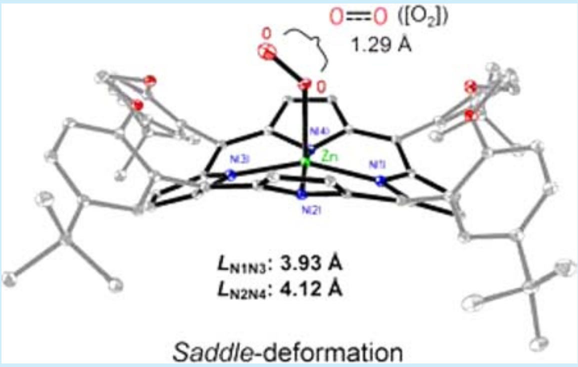
S Supporting Information

ABSTRACT: Three *saddle*-type nonplanar zinc porphyrins strapped by two short alkyl linkers have been synthesized. The deformation induced by the linkers can cause a spectral red shift of >30 nm compared with the absorption maxima of regular porphyrins and can also regulate the electronic structure of the central zinc(II) ion. The zinc(II) ion then complexes and activates a free dioxygen to form a superoxide group ligand by enlarging the splitting of energy levels of d orbitals under strong core deformation. The fixation of dioxygen can be reasonably explained by the Dewar−Chatt−Duncanson model. These results indicate that this type of saddle porphyrin has the potential to be used as a new model system of heme.



The use of dioxygen in oxidation reactions catalyzed by transition metals is relatively rare despite its enormous potential.[1] Indeed, the addition and activation of dioxygen by metallic compounds remains a largely immature field despite extensive literature on the subject, particularly regarding iron−[2,3]and copper−O_2 systems.[4,5] Porphyrinoids play a vital role in the oxidation processes of biological systems, e.g., the well-known heme, a porphyrin complex containing Fe.[6,7] Heme is sufficiently active to weaken the O−O bond of dioxygen and catalyze hydroxylation of inactivated C−H bonds.[8] The macrocyclic distortion of porphyrin in heme has been recognized as a conserved structural feature of particular proteins.[9,10]

Nonplanarity is universal to all heme proteins that bind NO or O_2.[11] Distorted heme can both stabilize the lower-valent Fe(II) oxidation state of the central iron species[12] and generate its higher-valent iron(IV, V)-oxo complex.[13] This distortion is energetically unfavorable, so it universality suggests that such conformational variation is crucial to the functions of metalloporphyrins and heme.[7,14] Nonplanar metalloporphyrins show many interesting properties, including potent catalytic ability,[15] variable coordination,[16] large spectral red shift,[17] tunable spin densities,[18] and other unusual physical properties.[19]

In heme chemistry, the electronic structure of the metal ion in a complex can undergo marked changes induced by a slight variation of the macrocycle.[20] One advantage of porphyrin macrocycles is that they are highly flexible and can adopt a range of nonplanar conformations that are needed for a variety of biological functions.[21] Recently, we demonstrated that the core contraction derived from a ruffling deformation of the porphyrin macrocycle can induce a conversion of the electronic structure of coordinated Fe(III).[22,23] Reports have also shown that zinc(II) species can be used as a catalyst in many oxidation reactions involving molecular oxygen[24] as well as in organic reactions.[25] These facts indicate that the activation of a metal to dioxygen possibly depends on its size but not necessarily on the presence of an odd electron. We developed an interest in what will occur in the filled d orbital of a Zn(II) ion under full contraction (strong deformation) of a macrocycle with an N_4 core. In the current report, three 5,10-15,20-distrapped zinc porphyrins **1**-Zn to **3**-Zn with *saddle*-type distortion are synthesized and characterized to determine the effect of this macrocyclic deformation on the electronic structure of the central zinc ion.

Distrapped materials **1**-Zn to **3**-Zn were obtained from the condensation of dialdehyde with pyrrole with a molar ratio of 1:2 in yields of 0.8−6.0% in refluxing propionic acid (Scheme 1).[26,27] The formation of this type of highly deformed macrocycle involves tandem reactions including condensation and oxidation and includes a pyrrole-containing intermediate bridged by straps $O(CH_2)_xO$ (x = 2, 3, and 4) at the two phenyl groups of the pyrrolyl α-positions (see Supporting Information p S6). The model compounds were directly characterized by X-ray diffraction, UV−vis and NMR spectral methods, and high-resolution mass spectrometry.

Macrocyclic distortion in porphyrins results in a spectral red shift, and the degree of distortion roughly depends on the magnitude of the shift.[28] For models **1**-Zn to **3**-Zn, as the degree of distortion increased, the maxima of the Soret band red-shifted from 429.5 to 450.0 nm (**3**-Zn → **1**-Zn), as shown

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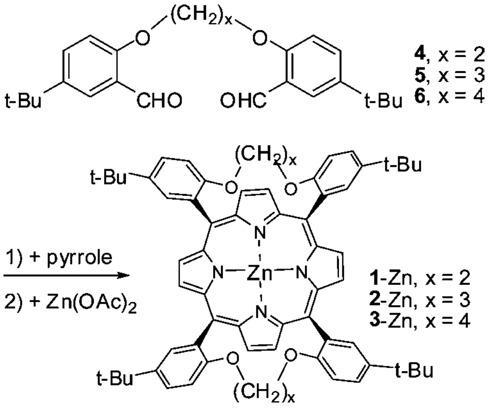
Scheme 1. Synthesis of Distrapped Zinc Porphyrin 1-Zn to 3-Zn



in Figure 1. The **1**-Zn tends to exist in the Zn$-$O$_2$ complex form which displays a red shift of 2.2 nm (Supporting Information p S3). The electronic spectra of **1**-Zn showed a red shift of >30 nm compared with those of regular porphyrins. The obvious shift indicates that there is considerable macrocyclic deformation that changes the ground state of the molecule.[27]

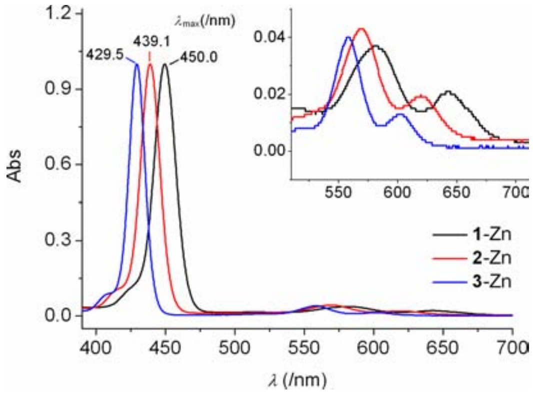


Figure 1. Absorption spectra of the distrapped zinc porphyrin **1**-Zn to **3**-Zn in CHCl$_3$ at 293 K. Insert is a magnified image of the Q-bands.

Inspection of crystal structures of **1**-Zn to **3**-Zn reveals that the macrocycle is strapped by two short alkyl groups, which compels the macrocycle to adopt a *saddle*-type deformation (Figure 2). An important feature of the current model systems composed of three zinc porphyrins is the continuous change in the degree of distortion. This conformation further makes the N$_4$ core deform from an approximate square in a regular system to a rhombus. One diagonal N$-$N distance (L_{N2N4}) is unchanged along the N2$-$N4 direction in the core and maintains a value of ~4.1 Å, whereas the distances of another direction (L_{N1N3}) considerably shorten to 3.93 Å in **1**-Zn. As a result, the difference between the two directions is up to ~0.2 Å. The changes are not a pure contraction or expansion like that observed for deformed porphyrins previously.[27,28]

The most remarkable difference of **1**-Zn from **2**-Zn and **3**-Zn is the axial ligands. The crystal structure of **1**-Zn contains a dioxygen ligand that is directly bonded to the zinc ion, whereas the more regular macrocycles of **2**-Zn and **3**-Zn contain methanol. This phenomenon has not been found previously, and the addition and activation of dioxygen by zinc reagents has not been reported, although the selective oxygenation of organozinc material with O$_2$ has been demonstrated,[25] and a hydroperoxo zinc(II) intermediate has also been obtained.[29] These findings prompted us to focus on the relationship between the ligation of dioxygen and macrocyclic deformation. Note that the complex **1**-Zn-O$_2$ is surprisingly stable, and the O$_2$ ligand cannot be removed by a Lewis base like pyridine under the current spectral conditions.

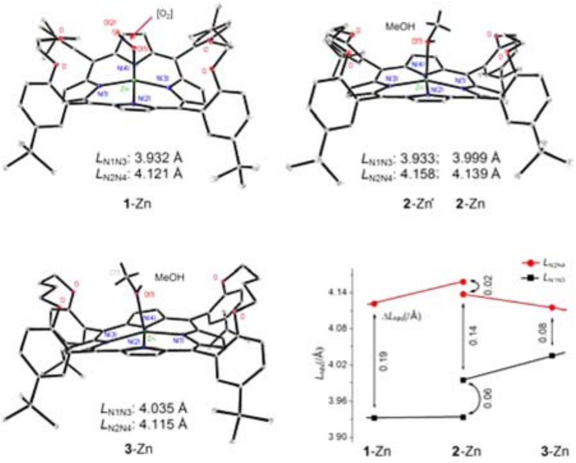


Figure 2. Crystal structures of *cis*-distrapped zinc porphyrins **1**-Zn to **3**-Zn. L_{NN} is the distance between the diagonal N atoms in the center of the macrocycle. Protons have been omitted for clarity apart from those of the axial ligands.

Metal$-$dioxygen complexes can usually be classified as superoxo and peroxo complexes according to their O$-$O bond parameters.[30] The X-ray structural analysis of **1**-Zn revealed an unusual O$-$O bond length (1.29 Å, Figure 3a) that is close to the range of superoxide compounds (1.30$-$1.33 Å).[31] The value is neither within the range for known metal peroxide complexes (1.40$-$1.52 Å)[32] nor equal to that of free dioxygen (~1.1 Å). This indicates that the axial O$_2$ has been converted to a superoxide group because the O$-$O bond length varies in this class of compounds.[33] The structural parameters of **3**-Zn are in line with a normal Zn$-$methanol assembly (Figure 3b).

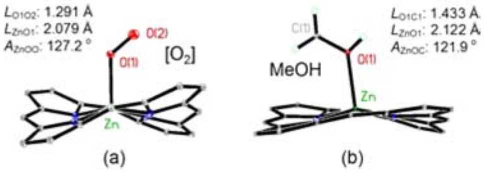


Figure 3. Bond parameters of axial ligands in (a) distrapped zinc porphyrin **1**-Zn, and (b) reference **3**-Zn. *L* represents bond length, and *A* represents bond angle.

A Dewar$-$Chatt$-$Duncanson (DCD) model established to explain organometallic compounds with chemical bonding between an alkene and metal[34,35] can perfectly explain the formation of the O$_2$$-$zinc porphyrin complex **1**-Zn-O$_2$. A report showed that dioxygen can be activated via formation of an oxo-osmium(IV) π-complex.[36] **1**-Zn-O$_2$ is also a type of π-complex. In **1**-Zn-O$_2$, the lone electron pair of the terminal O atom, rather than the π electron in the oxo-osmium(IV) complex above,[37] of dioxygen donates an electron pair to a zinc d-orbital to form a σ-coordination bond (Figure 4a-I). The

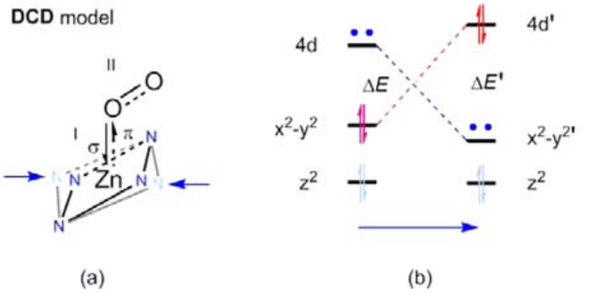


Figure 4. (a) The Dewar−Chatt−Duncanson (DCD) model to rationalize complex **1**−Zn-O_2, and (b) the change of electronic structure of the coordinated zinc ion under core deformation of the macrocycle. The blue arrows denote the compression.

metal consequently donates electron density back from a different filled d-orbital into the empty antibonding orbital (π^*) of dioxygen (Figure 4a-II) to form a π-coordination bond (named a feedback π bond). Both of these effects tend to increase the Zn−O bond order and decrease that of the O−O bond, leading to a shortened Zn−O distance and elongated O−O one.

The bond parameters of the axial ligands in **1**-Zn and **3**-Zn fully support the above analysis (Figure 3). In complex **1**-Zn-O_2, the O−O bond length has increased to 1.29 Å from 1.06 Å in free dioxygen. At the same time, the Zn−O bond is strengthened and the bond length is 2.08 Å, which is 0.04 Å shorter than the 2.12 Å in regular zinc porphyrin **3**-Zn. This interaction also tends to cause the coordinated oxygen atom to "rehybridize" from the sp^2 mode toward the sp one, which is evidenced by the larger bond angle A_{ZnOO} of 127.2°.[38]

It has been demonstrated that macrocyclic deformation can induce conversion of electronic structure[22,23,39] and regulate splitting[40] of d-electron energy levels of some metal ions in deformed porphyrins (Figure 4b). Unlike the single conformation **1**-Zn and **3**-Zn, the crystal of **2**-Zn includes four isomers divided into two groups according to the different sizes of the two diagonal directions, L_{N1N3} and L_{N2N4} (Supporting Information p S2), which means that isomers distinguished as **2**-Zn′ and **2**-Zn coexist and implies that the conversion size of the zinc ion in this electronic structure is the 3.93 Å of the N1−N3 distance.

In model complex **1**−Zn-O_2, the weakening of the O−O bond and strengthening of the Zn−O one mainly depend on the presence of a feedback π bond. The electron exchange process of a zinc ion is believed to be a necessary condition but not sufficient alone to form the feedback bond. The electron pair from the N_4 unit would cause the energy level of the $3d_{x^2-y^2}$ orbital to decrease and form the $(3d_{x^2-y^2})'$ orbital if the compression was great enough. Meanwhile, unlike in other metal ions such as Fe^{3+} and Co^{2+} that possess unsaturated orbitals, the electron pair of a zinc(II) ion in the original $3d_{x^2-y^2}$ orbital can only escape from all of the 3d orbitals (labeled in red in a possible 4d orbital) and is not allowed to enter one of lower energy. The shorter N−N distance of one diagonal in complex **1**-Zn-O_2 induces large enough splitting of the energy level between a 4d′ orbital and $(3d_{x^2-y^2})'$ one. The excluded electron pair is activated and tends to be donated. In brief, the main role of core deformation is to make the energy level of the 4d′ orbital rise to match that of the antibonding (π^*) orbital of O_2 to allow electron transfer between the orbitals and form the feedback bond.

The superoxide moiety is influenced by bonding with the metal ion. The presence of the feedback π bond in this complex should facilitate cleavage of the O−O bond in the superoxide group, which is directly supported by HR-MS data. Under the conditions of electrospray ionization mass spectrometry (ESI MS), two signals for the **1**-ZnO and **1**−Zn-O_2 segments as well as that from **1**-Zn (Figure 5 I) predominantly occurring in planar systems are readily observed in the spectrum of **1**-Zn-O_2. This signal (Figure 5 II) can only be interpreted as cleavage of the O−O bond.

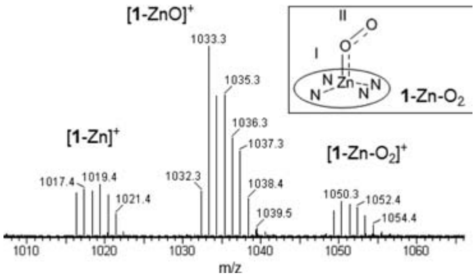


Figure 5. Mass spectrum of zinc porphyrin complex **1**-Zn-O_2.

In conclusion, the synthesis of a highly distorted O_2−Zn porphyrin complex that demonstrates the activation mechanism of deformed zinc ions to molecular dioxygen was reported here. The results indicate that the fixation of oxygen can be independent of the oxidation of oxygen in heme. Further studies on the oxygenation of the activated dioxygen in such complexes are in progress. Our results indicate that zinc has the potential to activate dioxygen only in suitably deformed porphyrins, further implying the importance of macrocyclic distortion in heme.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02010.

Experimental details and NMR, HR-MS, and IR data (PDF)
Crystallographic data for **1**-Zn (CIF)
Crystallographic data for **2**-Zn (CIF)
Crystallographic data for **3**-Zn (CIF)

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Notes

The authors declare no competing financial interest.

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