Iron Porphyrinoids

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Nitrosylation in a Crystal: Remarkable Movements of Iron Porphyrins Upon Binding of Nitric Oxide**

Nan Xu, Douglas R. Powell, and George B. Richter-Addo**

Iron porphyrins are important cofactors in various heme enzymes and biomolecules. While much is known about the consequences of histidine (His) coordination to the heme iron center, much less is known about the related effects the coordination of an O-donor ligand to the iron center in heme compounds. Such O-ligand binding is present in the active site of heme-containing catalase where the side-chain of a protein tyrosine (Tyr) provides the O coordination.[1] Related Tyr O coordination has recently been discovered to be a critical factor in the important class of heme-binding HasAp proteins.[2] Some naturally occurring hemoglobin mutants such as HbM Iwate and Hb Hyde Park exhibit O coordination from endogenous Tyr side chains.[3] The increased attention that such heme/O-ligand complexes have attracted warrants new studies to examine their axial binding of exogenous diatomic ligands. For example, it is known that the vasodilator nitric oxide (NO) can inhibit the function of heme catalase presumably by direct binding of NO to iron;[4] the Cat^{III}(NO) compound has been reported,[5] as has the Cat^{II}(NO) derivative.[6]

It is surprising that there are no reported crystal structures of NO adducts of Tyr-ligated heme proteins. Even more surprising is that there are only two reported crystal structures of synthetic [(por)Fe(NO)(O-ligand)] (por = porphyrin) compounds, namely [(TPP)Fe(NO)(H_2O)]ClO_4[7] and [(TPP)Fe(NO)(HO-i-C_5H_{11})]ClO_4 (TPP = tetraphenylporphyrin);[8] the former was obtained through the reaction of a $CHCl_3$/benzene (5:2) solution of [(TPP)Fe(H_2O)$_2$]ClO_4 with NO gas and the latter obtained by serendipity when isoamyl alcohol was reacted with a CH_2Cl_2 solution of [(TPP)Fe(THF)$_2$]ClO_4. This paucity of structural information on the [(por)Fe(NO)(O-ligand)] species is due in a large part to the general instability of the ferric–NO bond and ready reductive conversion into the ferrous–NO derivatives in the presence of excess NO. We previously reported the preparation of a heme nitrosyl thiolate compound using a unique solid-gas reaction that allowed X-ray structural characterization.[9] Herein, we report that we have utilized gaseous diffusion of NO into a suitably constructed crystal of the five-coordinate precursor [(TPP)Fe(H_2O)]SO_3CF_3 (**1**) to generate the nitrosyl derivative as determined by IR spectroscopy and single-crystal X-ray crystallography. This solid-gas reaction permits, for the first time, a detailed structural comparison between the precursor compound and its NO adduct in the same crystal under identical experimental conditions.

Exposure of several hand-picked crystals of **1**[10] to NO gas (1 atm) at room temperature for 12 hours under an anaerobic atmosphere resulted in the generation of the derivative **2**, which was characterized by a new band in the IR spectrum at $\tilde{\nu} = 1897\ \text{cm}^{-1}$, which was attributed to ν_{NO}. We then used these crystal derivatives for an X-ray diffraction study. The molecular structure of the NO adduct derived from exposure of the crystal to NO is shown in Figure 1, and the packing diagram of the product is shown in Figure 2. The structure reveals that the product is a mixture of the precursor five-coordinate complex **1** (Figure 2, top) and its NO derivative **2** (Figure 2, bottom) in a 1:1 ratio and allows a reliable comparison of the structural parameters between the NO ligated (**2**) and unligated (**1**) complexes.

There are several important points to note about the structures of **1** and its nitrosyl adduct **2**. First, only half the number of molecules of the five-coordinate complex **1** were nitrosylated at Fe. The porphyrin faces that bind NO are those that did not have the axial H_2O ligand stabilized by hydrogen-bonding with triflate (see also the structure of isolated **1** in Figure S1 in the Supporting Information). The changes in crystal packing upon NO binding to **1** reveals dramatic movements of the molecules in this crystal without sacrificing

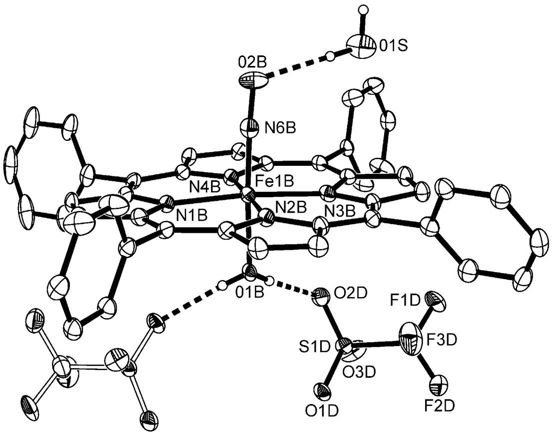

Figure 1. Molecular structure of the [(TPP)Fe(NO)(H_2O)]SO_3CF_3 (**2**) component from the 1:1 product mixture of **1** and **2**. Thermal ellipsoids drawn at 35% probability. The dashed lines represent the hydrogen-bonding interactions of the aquo ligand and nitrosyl group with the two triflate anions and a water molecule, respectively.

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[*] Dr. N. Xu, Dr. D. R. Powell, Dr. G. B. Richter-Addo
Department of Chemistry and Biochemistry
University of Oklahoma
101 Stephenson Parkway, Norman, OK 73019 (USA)
E-mail: xunan@ou.edu
grichteraddo@ou.edu

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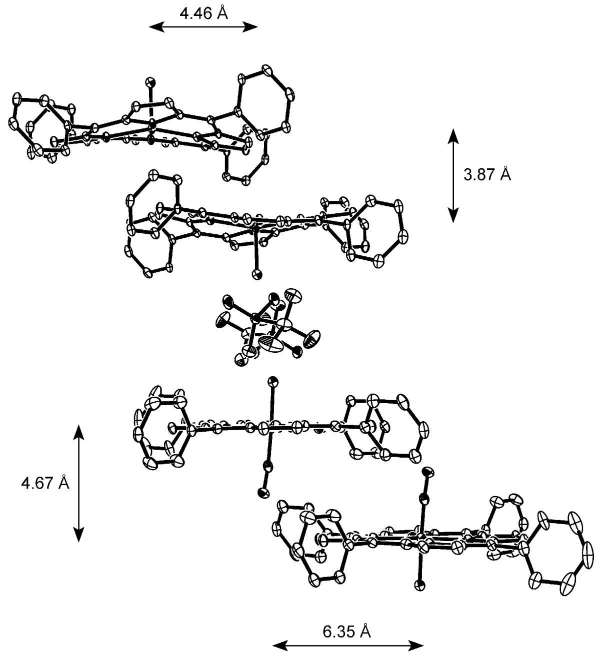

Figure 2. The packing diagram showing the relative positioning of $[(TPP)Fe(H_2O)]SO_3CF_3$ (**1**; top) and $[(TPP)Fe(NO)(H_2O)]SO_3CF_3$ (**2**; bottom) in the 1:1 product mixture from the NO diffusion reaction of **1**. Thermal ellipsoids drawn at 35 % probability. The triflate anions for the porphyrin cations have been omitted for clarity.

crystal diffraction quality. Diffusion of NO into the crystal lattice disrupts the π–π interaction between two adjacent porphyrin rings by essentially pushing the pair of porphyrin molecules apart (bottom pair of compounds in Figure 2), with a distance of 6.98 Å between adjacent nitrosyl O atoms, thus indicating no direct interaction between these atoms. As shown in the bottom portion of Figure 2, the porphyrin mean plane separation (M.P.S.) is 4.67 Å, thus showing a remarkable increase from the 3.88 Å shown for **1** (see Figure S2 in the Supporting Information) to accommodate the new NO ligand; the lateral shift (L.S.) also increases from 4.43 Å in precursor **1** to 6.35 Å in **2** to accommodate this NO ligand. The non-nitrosylated porphyrins remain in essentially the same relative position with a lateral shift of 3.87 Å and M.P.S. of 4.46 Å (see Figure S2 in the Supporting Information). The unit-cell volume of the nitrosylated product (with two molecules in the asymmetric unit) is 3818.2(16) $Å^3$ which is larger than the volume of two unit cells (one molecule in the asymmetric unit; $V = 1833.4(3)$ $Å^3$) in the unreacted crystal of **1** (see Figures S3 and S4 in the Supporting Information). This volume change reflects the expansion of the molecular volume caused by the addition of NO to half the number of the ferric centers.

Second, NO binds in a linear fashion to the ferric centers (∡FeNO = 173.0(3)°), and the porphyrin macrocycle in **2** is essentially flat (Figure 2, bottom) whereas it is saddled in **1** (Figure 2, top; Figure S2 in the Supporting Information). Further, the Fe–N(por) bond lengths in **2** are in the narrow 2.001(3)–2.006(3) Å range and are longer than the 1.972(2)–1.989(2) Å range in complex **1**.[12] This correlates with Fe moving into the porphyrin plane in **2** ($\Delta Fe = +0.05$ Å relative to the 24-atom plane) from its −0.24 Å displacement towards the aquo ligand in **1**. This translates to a 0.29 Å vertical movement of Fe in the intact crystal during the nitrosylation experiment. In addition, the trans Fe–O bond in **2** (1.961(3) Å) is shorter than the Fe–O bond in the five-coordinate **1** (2.012(2) Å) and that in the six-coordinate high-spin $[(TPP)Fe(H_2O)_2]^+$ (2.095 Å);[13] this shortening of the trans Fe–O bond upon NO binding is probably a consequence of the negative trans influence of NO in compounds exhibiting a high ν_{NO}.[14,15] Third, we observe evidence for hydrogen bonding of the nitrosyl O atom of the linear NO ligand with a low-occupancy fixed water molecule ($FeNO\cdots OH_2 = 3.05$ Å; 17 % occupancy). It is interesting to note that no fixed nonligated water molecules are evident in the crystal structure of **1**, although it was prepared in the presence of excess water. It is likely that, if present, these water molecules may be highly disordered and thus not observable by our X-ray diffraction experiment. The appearance of the fixed water molecule hydrogen bonded to NO in the crystal structure of **2** is probably the result of the hydrogen-bonding-induced restriction of its movement in the vicinity of the NO ligand. There is precedent for hydrogen bonding to nitrosyl O atoms.[14] For example, Belkova and co-workers reported the formation of a hydrogen bond between the nitrosyl O atoms of $[Re(NO)(CO)(PR_3)_2(H)_2]$ (R = Me, Et, *i*Pr) and $(F_3C)_3COH$ molecules.[19] Analogous hydrogen bonding of H_2O molecules to nitrosyl O atoms of ferrous [(por)Fe(ImH)(NO)] compounds containing bent NO ligands has been examined computationally.[20]

In summary, we have employed a rare solid-gas two-phase reaction to obtain and structurally characterize the NO adduct of a crystalline [(por)Fe(O-ligand)] species. The NO binding to only half the number of ferric centers results in a remarkable movement of the porphyrin molecules within a solid crystal without sacrificing X-ray diffraction quality.

Experimental Section

Degassed distilled water (0.02 mL) was added to a CH_2Cl_2 solution (10 mL) of $[(TPP)Fe(OSO_2CF_3)]$[21] (20 mg, 0.024 mmol). The mixture was stirred for 20 min, during which time the color changed from brown-red to brown. Cyclohexane (5 mL) was added and the solution was left to evaporate under N_2 at room temperature. Black crystals of the product $[(TPP)Fe(H_2O)]SO_3CF_3$ (**1**) were obtained (0.022 mmol, 90 % yield). The IR spectrum of **1** shows, in addition to the porphyrin bands, the characteristic bands of an uncoordinated triflate anion at 1295 cm^{-1} ($\nu_{as}(SO_3)$), 1226 cm^{-1} ($\nu_s(CF_3)$), 1168 cm^{-1} (shoulder, $\nu_{as}(CF_3)$), and 1022 cm^{-1} ($\nu_s(SO_3)$).[22] Crystals of **1** were grown from CH_2Cl_2/cyclohexane (2:1) at room temperature.[23] The molecular structure and packing diagram of **1** are shown as Figures S1 and S2, respectively, in the Supporting Information. The unit cells of **1** and **2** are shown as Figures S3 and S4, respectively. The stacking diagram of **1** revealing a possible channel for NO diffusion into the crystal is shown as Figure S5.

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[10] The molecular structure of **1** is shown in Figure S1 in the Supporting Information and clearly reveals a five-coordinate Fe center, with the axial water in hydrogen-bonding contact with the triflate anions; hydrogen bonding to the triflate anions are shared between pairs of $[(TPP)Fe(H_2O)]^+$ cations. We note that Scheidt and co-workers reported the preparation of the related six-coordinate $[(TPP)Fe(H_2O)_2]ClO_4$ complex from the reaction of the oxo-dimer $[(TPP)Fe]_2(\mu\text{-}O)$ with aqueous perchloric acid.[11] The isolation of **1** as a crystalline five-coordinate mono-aquo complex is consistent with the observed π–π interaction (see Figure S2 in the Supporting Information) between two adjacent porphyrin rings that does not readily allow hydrogen bond stabilization of a second coordinated H_2O molecule either by the triflate anion or by solvent.

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[12] The $Fe{-}N_{por}$ bond length increases from 1.982(2) Å to 2.004(3) Å upon NO ligation; the average $Fe{-}N_{por}$ is comparable to the 1.999(6) Å value observed in low-spin $[(TPP)Fe(H_2O)(NO)]ClO_4$.[7] The spin state of five-coordinate $[(TPP)Fe(H_2O)]^+$ is unknown. However, the spin state of the closely related five-coordinate $[(OEP)Fe(H_2O)]^+$ (OEP = octaethylporphyrin) has been determined as admixed intermediate spin on the basis of its temperature-dependent magnetic susceptibility data: B. Cheng, M. K. Safo, R. D. Orosz, C. A. Reed, P. G. Debrunner, W. R. Scheidt, *Inorg. Chem.* **1994**, *33*, 1319–1324.

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[23] Crystal data for **1**: $C_{45}H_{30}F_3FeN_4O_4S$ ($M_r = 835.64$), triclinic, space group $P\bar{1}$, $a = 11.0712(11)$, $b = 12.8780(13)$, $c = 13.7358(14)$, $\alpha = 78.282(2)$, $\beta = 81.182(3)$, $\gamma = 73.997(3)$, $V = 1833.4(3)$ Å^3, $Z,Z' = 2,1$, $T = 100(2)$ K, $R1 = 0.0620$ ($I > 2\sigma(I)$), $wR2$ (all data) = 0.1493. Crystal data for **2**: $C_{90}H_{60.34}F_6Fe_2N_9O_{9.17}S_2$ ($M_r = 1704.35$), triclinic, space group $P\bar{1}$, $a = 10.977(3)$, $b = 12.973(3)$, $c = 28.568(6)$, $\alpha = 78.137(6)$, $\beta = 89.734(6)$, $\gamma = 73.848(7)$, $V = 3818.2(16)$ Å^3, $Z,Z' = 2,1$, $T = 100(2)$ K, $R1 = 0.0672$ ($I > 2\sigma(I)$), $wR2$ (all data) = 0.1774. CCDC 823547 (**1**) and 823546 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.