A Stable Hyponitrite-Bridged Iron Porphyrin Complex

5 **AUTHORS**, INCLUDING:

George Richter-Addo
University of Oklahoma
125 PUBLICATIONS **2,395** CITATIONS

# A Stable Hyponitrite-Bridged Iron Porphyrin Complex

Nan Xu, **Adam L. O. Campbell**, **Douglas R. Powel**, **Jana Khandogin**[*], and **George B. Richter-Addo**[*]

Department of Chemistry and Biochemistry, University of Oklahoma, 620 Parrington Oval, Norman, OK 73019

Abstract

The coupling of two nitric oxide (NO) molecules in heme active sites is an important contributor to the conversion of NO to nitrous oxide (N_2O) by heme-containing enzymes. Several formulations for the presumed heme-$Fe\{N_2O_2\}^{n-}$ intermediates have been proposed previously, however, no crystal structures of heme-$Fe\{N_2O_2\}^{n-}$ systems have been reported to date. We report the first isolation and characterization of a stable bimetallic hyponitrite iron porphyrin, $[(OEP)Fe]_2(\mu-N_2O_2)$, prepared from the reaction of the $[(OEP)Fe]_2(\mu-O)$ with hyponitrous acid. Density functional calculations were performed on the model compound $[(porphine)Fe]_2(\mu-N_2O_2)$ to characterize its electronic structure and properties.

Heme-assisted coupling of nitric oxide (NO) to form $Fe\{N_2O_2\}^{n-}$ intermediates plays an important part in the reduction of NO to N_2O.[1,2] In transition-metal chemistry, such metal $\{N_2O_2\}^{n-}$ moieties can be generated from attack of NO on a metal-NO group,[3,4] from metal-induced coupling of NO,[5] or from transfer of an intact $(N_2O_2)^{n-}$ from a diazeniumdiolate to a metal.[6] It is interesting to note that only a small number of metal$\{N_2O_2\}$-containing compounds have been structurally characterized, and the $\{N_2O_2\}$ binding modes determined to date are sketched below as structures **A** (M = Pt, Ni),[5,6] **B** (M = M' = Co),[7] **C** (M = Ru)[8] and **D** (M = Co).[9]
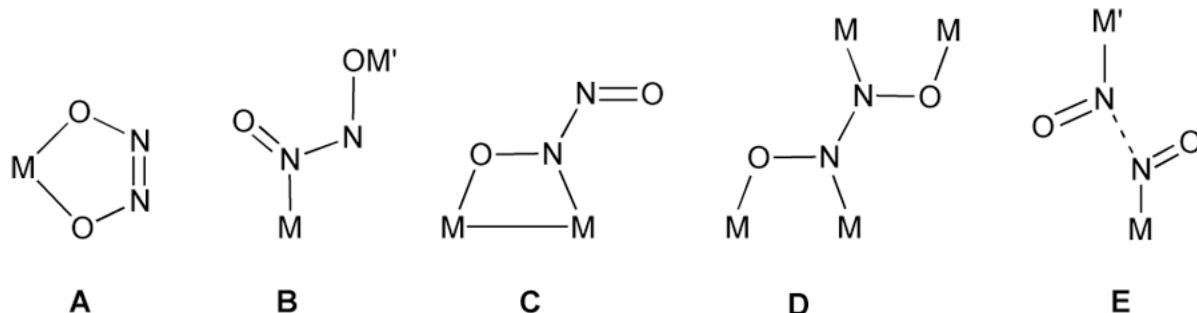
Enzymes such as the NO reductase (NOR) from *Paracoccus denitrificans*, cyt *ba*$_3$ and *caa*$_3$ from *Thermus thermophilus*, and cyt *cbb*$_3$ from *Paracoccus stutzeri* catalyze the conversion of NO to N_2O using bimetallic active sites.[1,2] For these biological systems, intermediates resembling structure **B** have been proposed, where the metal$\{N_2O_2\}$ moiety is *N*-bound to heme Fe (M), and where M' (non-heme Fe or Cu) may contact both O atoms.[1,10] Collman *et al.* have proposed, using results from the reaction of a diferrous synthetic model of NOR with NO, that a *trans* bis-nitrosyl intermediate forms at the active site of NOR followed by NO coupling (structure **E**) to give N_2O and a bis-ferric product.[11] Resonance Raman spectroscopy

E-mail: jana.k.shen@ou.edu, E-mail: grichteraddo@ou.edu.

has been employed to assign a HONNO-bridged Fe-Cu species (i.e., a protonated analogue of **E**) during NO reduction by *T. thermophilus* cyt *ba*$_3$.[12] To the best of our knowledge, however, no adduct of heme and an N_2O_2 moiety has been structurally characterized.

The title compound was obtained from the reaction of $[(OEP)Fe]_2(\mu\text{-}O)$ in anhydrous toluene with an in situ-generated ether solution of hyponitrous acid (Supporting Information) (eq 1). Workup gave the product $[(OEP)Fe]_2(\mu\text{-}N_2O_2)$ (**1**) as dark purple microcrystals in 52% isolated yield.

$$[(OEP)Fe]_2(\mu - O) + H_2N_2O_2 \rightarrow [(OEP)Fe]_2(\mu - N_2O_2) + H_2O \tag{1}$$
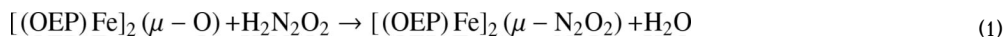
The IR spectrum of **1** reveals a band at 982 cm^{-1} assigned to υ_{as} of the N-O group (υ_{as}(^{15}NO) 973 cm^{-1}). This band is lower than that reported for $H_2N_2O_2$ at 1014/1003 cm^{-1} (υ_{as}(^{15}NO) 991/980 cm^{-1}).[13] The υ_s(NO) and υ(NN) bands were not observed in the IR spectrum, presumably due to the symmetry of **1**. The EPR spectrum of **1** as a CH_2Cl_2/toluene glass (77 K) shows $g = 5.74$ and 2.03; similar data were obtained for high-spin (H.S.) ferric hydroxo porphyrins.[14]

The X-ray crystal structure of **1** reveals that the N_2O_2 ligand is bound to each Fe via the η^1-O binding mode and that the ONNO moiety is *trans* (Figure 1). The N–N bond length of 1.250 (3) Å suggests double bond character (*c.f.*, 1.256(2) Å in crystalline $Na_2N_2O_2$).[15] The distance between the two Fe centers is 6.7 Å, and is longer than the 4.4 Å distance between the Fe and Cu centers in *T. thermophilus* cyt *ba*$_3$ that exhibits NOR activity.[16] The magnitude of the Fe–N(por) bond lengths in **1** and the apical displacement of Fe from the 4N-atom porphyrin mean plane (ΔFe = 0.40 Å) are indicative of H.S. ferric Fe centers. It follows that the N_2O_2 ligand in **1** must have significant hyponitrite (i.e., dianionic) character.

To characterize the electronic structure and properties of **1**, we performed calculations using density functional theory (DFT) on the model compound $[(porphine)Fe]_2(\eta^1,\eta^1,\mu\text{-}N_2O_2)$ (**1-calc**) in the *trans* and *cis* configurations. The DFT calculations were based on the B3LYP exchange-correlation functional and a triple-zeta polarization basis set. In both *trans* and *cis* configurations, the H.S. species is calculated to be lower in energy relative to the intermediate-(I.S.) and low-spin (L.S.) variants by 8 and 19 kcal/mol, respectively (Table S2). The calculated geometry of the *trans* H.S. species most closely reproduces the crystal structural data (Table 1). Curiously, the different spin states of the *trans* isomer are calculated to be ~2 kcal/mol higher in energy than the respective *cis* variants. This small difference lies within the typical error of 3–5 kcal/mol estimated for B3LYP calculations of transition-metal complexes. Thus, the DFT calculations are consistent with the EPR and structural data in establishing the identity of a stable H.S. *trans* species. The small energy gap between the *trans* and *cis* configurations suggests that isolation of the *cis* derivative of **1** might be attainable.

To probe the charge distribution in **1**, we used multipole-derived population analysis for the *trans* H.S. form of **1-calc**. The atomic charges on the Fe, O and N atoms are shown in Figure 2. To further understand the charge distribution in the FeONNOFe moiety, we used the Nalewajski-Mrozek scheme to calculate the bond orders. Accordingly, the bond orders for Fe–O, O–N, and N–N in 1-calc *trans*-H.S. (Figure 2) are 0.79, 1.25, and 1.84, respectively, which supports the notion of an N=N double bond in the hyponitrite bridge.

The Kohn-Sham orbitals of the *trans* H.S. species of **1-calc** are expected to be similar to those of square pyramidal metal complexes, for which the highest occupied orbital and the lowest unoccupied orbital are the result of anti-bonding interactions between dz^2 as well as $d(x^2\text{-}y^2)$ orbitals of the metal and the symmetrized combinations of the ligand σ orbitals. The frontier spin orbitals from the unrestricted openshell calculation are shown in Figure 3. The highest

occupied α spin orbital exhibits more porphine character while the lowest unoccupied spin β orbital displays more metal character. The N atoms of the hyponitrite bridge form a bonding interaction in both highest occupied spin orbitals.

Protonation of a toluene solution of **1** at 0 °C using HCl results in the formation of N_2O and (OEP)FeCl (eq 2). An IR

$$[(OEP)Fe]_2(\mu - ONNO) + 2HCl \rightarrow N_2O + 2(OEP)FeCl + H_2O \tag{2}$$
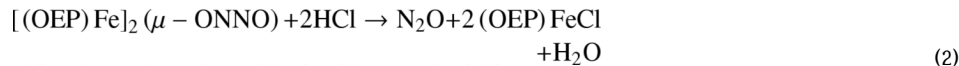
spectrum of the headspace reveals new bands at 2236/2213 and 1298/1266 cm^{-1} assigned to υ_{as} and υ_s of N_2O, respectively. The use of the ^{15}N-labeled **1** (labeled at hyponitrite) shifts the υ_{as} bands to 2167/2144 cm^{-1}; the corresponding υ_s bands were not observed due to its occurrence outside the detection window.

We hypothesized that the protonation reaction is initiated by H^+ attack on one of the O atoms of the hyponitrite bridge followed by O–N bond cleavage to give N_2O. This is supported by the pronounced negative charge on the hyponitrite O atom in *trans*-H.S. **1**-calc obtained from the DFT calculation. Further studies are underway to uncover the mechanism of the protonation reaction.

In summary, we have prepared and characterized the first isolable hyponitrite iron porphyrin complex, and describe the first established hyponitrite *O*-bonding mode to a heme model.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

References

1. Moenne-Loccoz P. Nat. Prod. Rep 2007;24:610–620. [PubMed: 17534533]

2. Yeung N, Lu Y. Chem. Biodiversity 2008;5:1437–1454.

3. Franz KJ, Lippard SJ. J. Am. Chem. Soc 1999;121:10504–10512.

4. Schneider JL, Carrier SM, Ruggiero CE, Young VG, Tolman WB. J. Am. Chem. Soc 1998;120:11408–11418.

5. Arulsamy N, Bohle DS, Imonigie JA, Moore RC. Polyhedron 2007;26:4737–4745.

6. Arulsamy N, Bohle DS, Imonigie JA, Levine S. Angew. Chem. Int. Ed 2002;41:2371–2373.

7. Villalba MEC, Navaza A, Guida JA, Varetti EL, Aymonino PJ. Inorg. Chim. Acta 2006;359:707–712.

8. Bottcher H-C, Graf M, Mereiter K, Kirchner K. Organometallics 2004;23:1269–1273.

9. Bau R, Sabherwal IH, Burg AB. J. Am. Chem. Soc 1971;93:4926–4928.

10. Blomberg LM, Blomberg MRA, Siegbahn PEM. Biochim. Biophys. Acta 2006;1757:31–46. [PubMed: 16375849]

11. Collman JP, Dey A, Yang Y, Decreau RA, Ohta T, Solomon EI. J. Am. Chem. Soc 2008;130:16498–16499. [PubMed: 19049449]

12. Varotsis C, Ohta T, Kitagawa T, Soulimane T, Pinakoulaki E. Angew. Chem. Int. Ed 2007;46:2210–2214.

13. McGraw GE, Bernitt DL, Hisatsune IC. Spectrochim Acta 1967;23A:25–34.

14. Cheng R-U, Latos-Grazynski L, Balch AL. Inorg. Chem 1982;21:2412–2418.

15. Arulsamy N, Bohle DS, Imonigie JA, Sagan ES. Inorg. Chem 1999;38:2716–2725.

16. Soulimane T, Buse G, Bourenkov GP, Bartunik HD, Huber R, Than ME. Embo J 2000;19:1766–1776. [PubMed: 10775261]

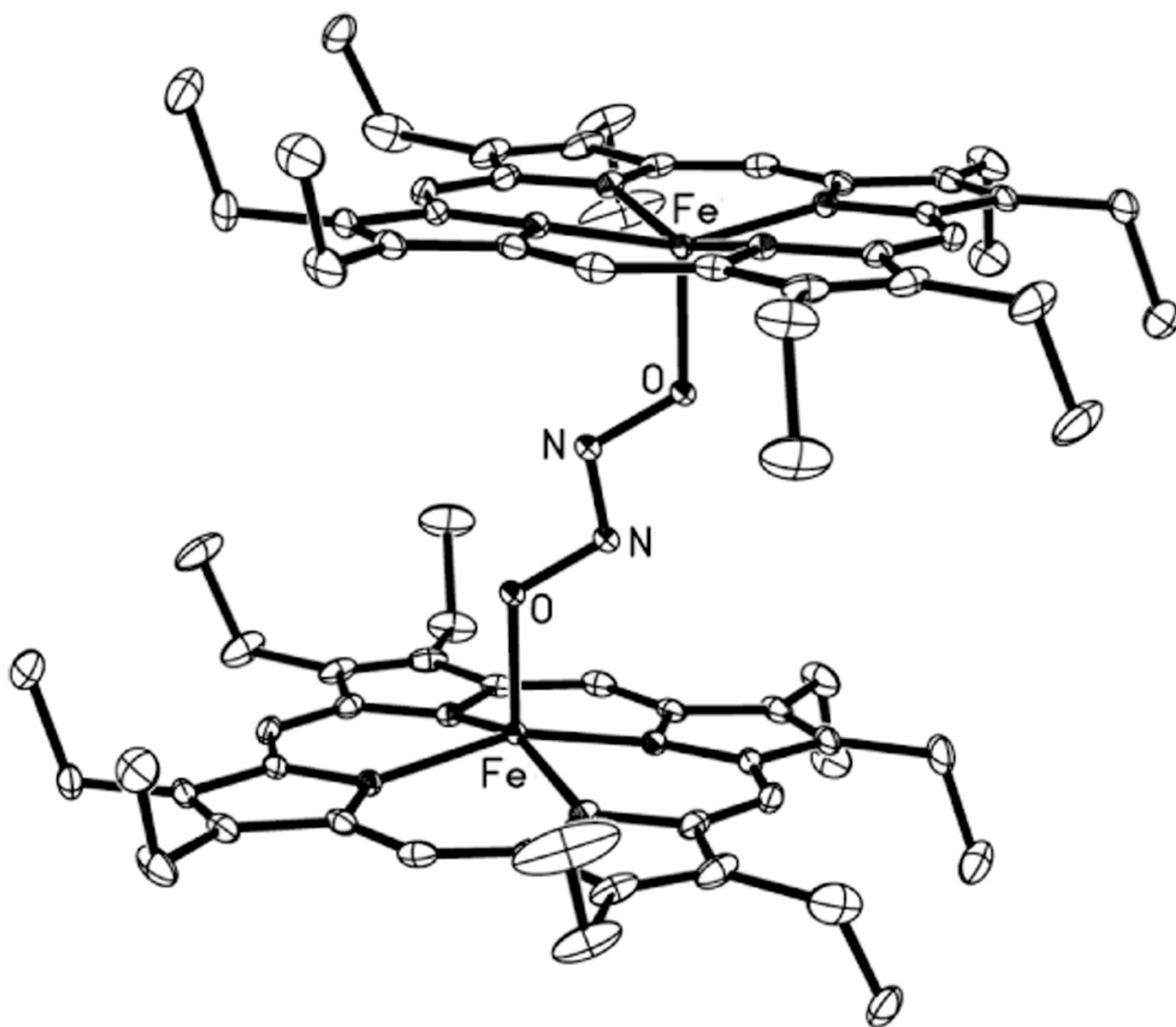**Figure 1.**
Molecular structure of [(OEP)Fe]$_2$(μ-ONNO) (**1**). Hydrogen atoms and the dichloromethane solvates have been omitted for clarity. Selected bond lengths (Å) and angles (°): Fe–O = 1.889 (2), O–N = 1.375(2), N–N = 1.250(3), Fe–N(por) = 2.049(2)–2.064(2), ∠FeON = 118.56(12), ∠NNO = 108.5(2).
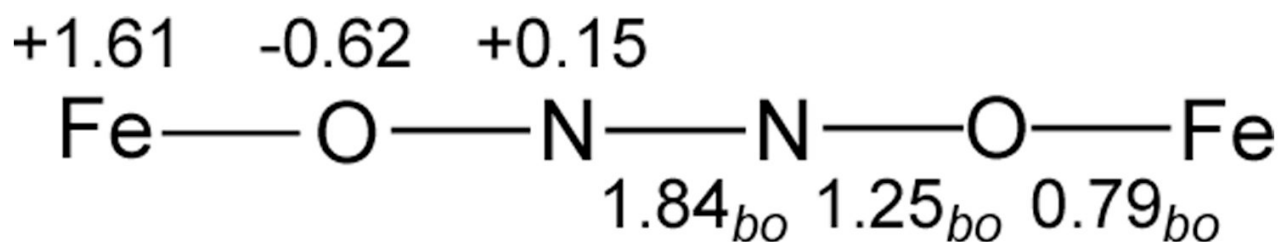
Figure 2.
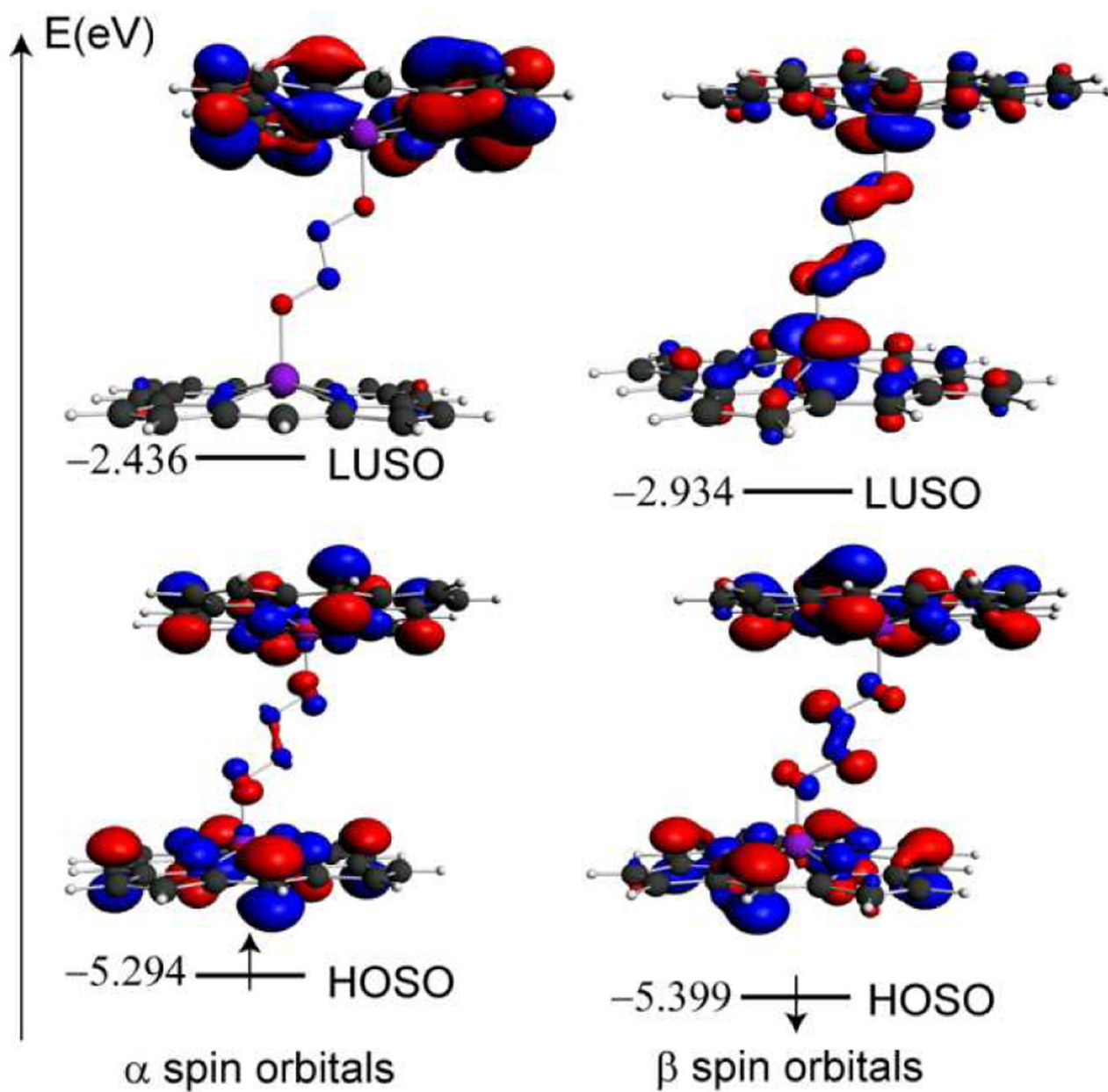Calculated atomic charges and bond orders (*bo*) for the FeONNOFe moiety.

Figure 3.
Frontier spin orbitals for high-spin **1**-calc. HOSO and LUSO denote the highest occupied and the lowest unoccupied spin orbitals, respectively.

Table 1

Selected crystal data for **1**, and calculated geometry data (in Å and °) for [(porphine)Fe]$_2$(η^1,η^1,μ-N$_2$O$_2$)(**1**-calc).

	Fe–O	O–N	N–N	∠NNO	ΔFe
1 (crystal; *trans*)	1.889	1.375	1.250	108.5	0.402
1-calc					
trans-H.S.	1.909	1.376	1.269	108.9	0.482
trans-I.S.	1.951	1.364	1.280	109.3	0.272
trans-L.S.	1.831	1.398	1.266	107.4	0.249
cis-H.S.	1.899	1.390	1.254	117.0	0.485
cis-I.S.	1.945	1.379	1.262	117.9	0.279
cis-L.S.	1.831	1.403	1.258	116.5	0.232