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Metalloporphyrins with X[N_2O_2]$^-$ Ligands. Novel High-Spin (*N*-Phenyl-*N*-nitrosohydroxylaminato)(*meso*-tetraarylporphyrinato)iron(III)

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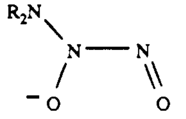
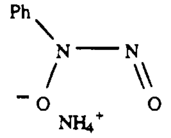
Nitric oxide (NO) is an important bioregulatory agent,[1] and structural studies of the interactions of hemes and heme models with NO have played a major role in elucidating the mechanism of activation of the NO-receptor enzyme guanylate cyclase.[2] Emphasis has also been placed on various NO carriers and how such entities function to release NO. Excellent work by Keefer and co-workers has shown that the Drago $R_2N[N_2O_2]^-$ anions ("NONOates") are smooth nonenzymatic releasers of nitric oxide in physiological media.[3] NONOates dilate blood vessels in rabbit aorta, show cytostatic activity in human cancer cells in culture, and have a potential for genotoxic action.[3a] The structurally related cupferron, $Ph[N_2O_2]NH_4$, is a common analytical reagent[4] and has also been shown to be carcinogenic in Fisher 344 rats and B6C3F1 mice, causing incidences of circulatory hemangiosarcomas.[5,6] We have been interested in the perhaps remote possibility that heme may play a role in the binding and activation of such $X[N_2O_2]^-$ groups (X = R_2N, Ph; R = alkyl). Despite the keen interest in the biological activity of such groups, there were no reports on how they could bind (unidentate or bidentate) to the iron centers in hemes or heme models prior to this study. We now report our successful synthesis and crystallographic characterization of the first thermally stable metalloporphyrin complexes containing the $X[N_2O_2]^-$ functional group.



NONOate



Cupferron

To a stirred CH_2Cl_2 (40 mL) solution of (TPP)FeCl (0.500 g, 0.710 mmol)[7] under an atmosphere of nitrogen was added AgON(Ph)NO[8] (0.162 g, 0.710 mmol). The solution was stirred for 10 min, and the red product mixture was filtered to remove precipitated AgCl. The volume of the filtrate was reduced in vacuo to ca. 20 mL; then hexane (10 mL) added, and the mixture was kept at −20 °C overnight. The resulting solid was collected by filtration and dried in vacuo to give (TPP)Fe(η^2-ON(Ph)-NO)·0.1CH_2Cl_2 (**1**·0.1CH_2Cl_2; 0.428 g, 0.526 mmol, 74% yield) as analytically pure dark purple crystals.[9] The observed magnetic moment of 5.84 μ_B indicates a formal high-spin Fe(III) center for this complex in benzene solution. The methoxy derivative (T(p-OCH_3)PP)Fe(η^2-ON(Ph)NO) (**2**) was obtained similarly in 65% yield.[9b,10]

In order to unambiguously determine the mode of linkage of the cupferron ligand toward the iron centers in these compounds, we subjected crystals to single-crystal X-ray crystallographic analyses.[11] The molecular structure of **2** is shown in Figure 1. The most chemically interesting feature of the structure is that the cupferron ligand is bound to the formally six-coordinate Fe(III) center in a bidentate σ-O fashion with an O−Fe−O bite angle of 71.52(9)° and with the Fe atom apically displaced 0.69 Å out of the plane of the 24-atom porphyrin ring (0.64 Å out of the plane of the porphyrin nitrogens). To the best of our knowledge, this is the largest mean displacement of an Fe atom from a porphyrin ring.[12,13] In the related structure of the *bidentate* nitrato complex (TPP)Fe(η^2-O_2NO) the Fe is drawn 0.60 Å out of the plane of the porphyrin ring (and 0.53 Å out of the plane of the four nitrogens of the porphyrin; O−Fe−O bite angle of 51.6(2)°).[14] The average Fe−O distance in the cupferron complex **2** is 2.068(3) Å. The cupferron N1−N2 bond length of 1.276(4) Å is shorter than that of a N−N single bond (1.45 Å) and is closer to that of a N=N double bond (1.25

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[7] TPP = *meso*-tetraphenylporphyrinato dianion; T(p-OCH_3)PP = *meso*-tetrakis(p-methoxyphenyl)porphyrinato dianion.

[8] Ahmed, M. A.; Edwards, A. J.; Jones, C. J.; McCleverty, J. A.; Rothin, A. S.; Tate, J. P. *J. Chem. Soc., Dalton Trans.* **1988**, 257.

[9] (a) Anal. Calcd for $C_{50}H_{33}N_6O_2Fe \cdot 0.1CH_2Cl_2$: C, 73.91; H, 4.11; N, 10.32; Cl, 0.87. Found: C, 73.75; H, 4.30; N, 10.29; Cl, 0.86. Low-resolution mass spectrum (FAB): *m/z* 806 [(TPP)Fe(ON(Ph)NO)]$^+$ (1%), 668 [(TPP)Fe]$^+$ (100%), 137 [ON(Ph)NO]$^+$ (37.7%), 107 [PhNO]$^+$ (39.6%). μ_{eff} = 5.84 μ_B. IR (KBr, cm^{-1}): $\nu_{ON(Ph)NO}$ 1292, 1285, 1204, 938 cm^{-1}. (b) Magnetic moments were measured on (6.0−10.8) × 10^{-3} M solutions in C_6D_6 at 21 ± 1 °C by the Evans method: Grant, D. H. *J. Chem. Educ.* **1995**, *72*, 39.

[10] Anal. Calcd for $C_{54}H_{45}N_6O_6Fe$: C, 69.75; H, 4.88; N, 9.04. Found: C, 69.51; H, 4.62; N, 8.83. Low-resolution mass spectrum (FAB): *m/z* 930 [(T(p-OCH_3)PP)Fe(ON(Ph)NO)]$^+$ (0.7%), 788 [(T(p-OCH_3)PP)Fe]$^+$ (100%). Low-resolution mass spectrum (DIP 70 eV): *m/z* 788 [(T(p-OCH_3)PP)Fe]$^+$ (3.6%), 107 [PhNO]$^+$ (67%). μ_{eff} = 5.92 μ_B.

[11] (a) Crystals of **2** (containing highly disordered solvent molecules) were grown from a CH_2Cl_2/hexane solution at −20 °C. Crystals are monoclinic, of space group $P2_1/n$, with a = 15.785(3) Å, b = 15.895(3) Å, c = 20.734(4) Å, β = 103.93 (3)°, V = 5049 (2) Å^3, Z = 4, and d(calcd) = 1.369 g cm^{-3}. The data were collected on a Siemens P4 diffractometer with Mo Kα radiation (λ = 0.710 73 Å) at 183 K. The data were corrected for Lorentz and polarization effects. No absorption correction was applied since it was judged to be insignificant. The structure was solved using the SHELXTL (Siemens) system and refined by full-matrix least squares on F^2 using all reflections (SHELXL-93).[11b] The structure was refined to a final conventional R1 = 0.0509 (wR2 = 0.1104, GOF = 1.045) for 5484 "observed" reflections with $I \geq 2\sigma(I)$. (b) Sheldrick, G. M. *Program for the Solution of Crystal Structures*; University of Göttingen: Göttingen, Germany; 1993. (c) The structure of **1** has also been determined, and is essentially isostructural with **2**. Details will be published in a full paper.

[12] (a) Scheidt, W. R.; Lee, Y. J. *Struct. Bonding* **1987**, *64*, 1. (b) Scheidt, W. R.; Reed, C. A. *Chem. Rev.* **1981**, *81*, 543.

[13] The structure of the N-methylated complex (*N*-CH_3TPP)FeCl reveals a 0.62 Å apical displacement of the Fe atom from the reference plane of the three unalkylated porphyrin nitrogens: Anderson, O. P.; Kopelove, A. B.; Lavallee, D. K. *Inorg. Chem.* **1980**, *19*, 2101.

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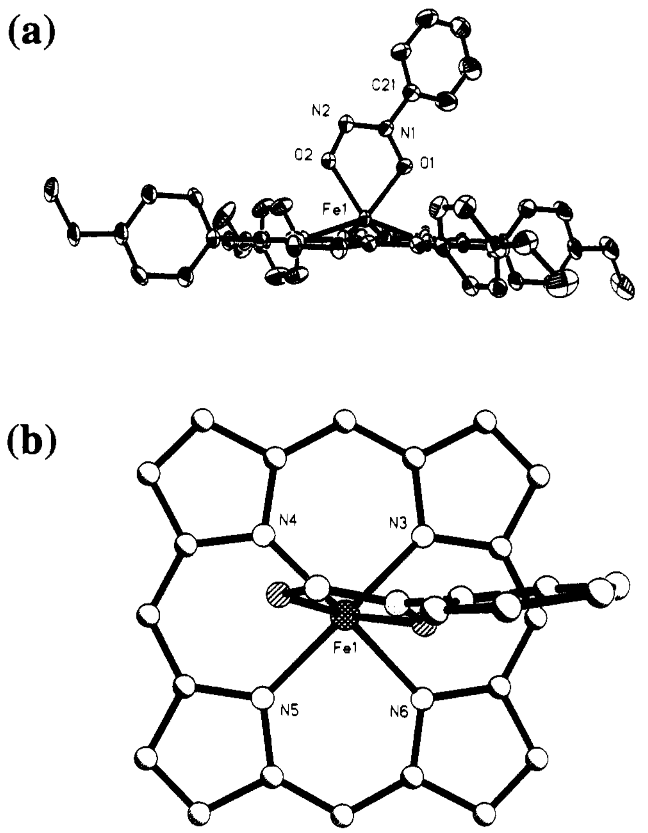

Figure 1. Two views of the molecular structure of $(T(p\text{-}OCH_3)PP)Fe(\eta^2\text{-}ON(Ph)NO)$ (**2**): (a) along the porphyrin plane; (b) perpendicular to the porphyrin plane (the anisole groups on the porphyrin are omitted). Hydrogen atoms have been omitted for clarity. The highly disordered solvent molecule is not shown. Selected bond distances (Å) and angles (deg): Fe1−O1 = 2.044(3), Fe1−O2 = 2.091(2), Fe1−N3 = 2.100(3), Fe1−N4 = 2.113(3), Fe1−N5 = 2.089(3), Fe1−N6 = 2.124(3), O1−N1 = 1.309(4), O2−N2 = 1.296(4), N1−N2 = 1.276(4); O1−Fe1−O2 = 71.52(9), N5−Fe1−O2 = 87.07(11), O1−Fe1−N3 = 84.52(11), N5−Fe1−N3 = 146.07(11), N5−Fe1−N4 = 85.85(11), O2−Fe1−N4 = 79.82(10), N3−Fe1−N4 = 83.72(11), N1−O1−Fe1 = 116.1(2), N2−O2−Fe1 = 119.7(2), N2−N1−O1 = 120.6(3), N1−N2−O2 = 111.5(3).

Å).[15] Furthermore, the average N−O bond length of 1.302(4) Å is between that of a single bond (1.40 Å) and double bond (1.21 Å).[15] These structural features suggest significant electron delocalization along the ON(Ph)NO moiety, a feature that is not uncommon for such groups.[8] The plane defined by the cupferron O1N1N2O2 atoms forms an angle of 83(1)° with the plane of the porphyrin nitrogens, and the cupferron phenyl group essentially eclipses a *meso*-carbon of the porphyrin ring (Figure 1b). The average Fe−N(porphyrin) bond length of 2.106(3) Å is indicative of a formal high-spin Fe(III) formulation for the complex in the solid state.[12b]

Interestingly, protonation of **1** by 1 equiv of triflic acid yields the known nitrosyl derivative (TPP)Fe(NO).[16-18] Several related points need to be mentioned. Scheidt and Wayland have employed some $X[N_2O_2]^-$ groups ($X = R_2N$) as active nitrosylating agents for the synthesis of nitrosyl metalloporphyrins, although no intermediate adducts of the form (porphyrin)$M(X[N_2O_2])$ were isolated.[18] Keefer and co-workers have studied the coordination chemistry of the $Et_2N[N_2O_2]^-$ anion with different metal centers, in particular with copper.[19] Coordination of this anion to the metal centers prolonged its lifetime in nonaqueous solution and resulted in varied extents of NO release per mole of metal complex. The copper complexes also exhibit vasorelaxant properties in vitro with isolated rabbit aorta.[19] Given the structural similarity of the NONOates and cupferron, the isolation and characterization of **1** and **2** thus suggest that such metalloporphyrin complexes with $X[N_2O_2]^-$ ligands may indeed be more accessible than previously thought.[20]

In summary, **1** and **2** are the first $X[N_2O_2]^-$ complexes of heme models to be reported. Mechanistic studies of protonation, and reactions designed for the activation of the bound cupferron ligands and related groups, are currently in progress. Importantly, the application of cupferron protonation for the synthesis of previously unknown metal nitrosyls is also being attempted.

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Supporting Information Available: Text giving experimental details for the crystal structure determination and refinement, structural drawings, and tables of crystallographic data, atomic coordinates, anisotropic thermal parameters, hydrogen coordinates, bond distances and angles, and least-squares plane data for $(T(p\text{-}OCH_3)PP)Fe(\eta^2\text{-}ON(Ph)NO)$ (**2**) (19 pages). Ordering information is given on any current masthead page.

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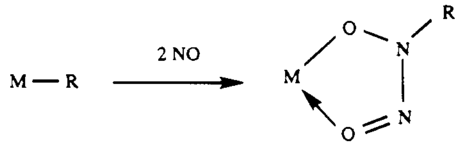
(16) In a typical reaction, triflic acid (0.010 g, 0.068 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a CH_2Cl_2 solution (30 mL) of **1** (0.055 g, 0.068 mmol). The color of the reaction mixture changed from reddish purple to brown purple. The (TPP)Fe(NO) product was precipitated with methanol (50 mL) and characterized by its IR spectrum: ν_{NO} (KBr) 1696 cm^{-1}. Low-resolution mass spectrum (FAB): *m/z* 668 $[(TPP)Fe]^+$. Typical yields range between 34 and 40%. The IR spectrum and GC of the reaction mixture established PhNO as the major organic product.

(17) The reaction of some rhodium cupferron complexes with HCl produces nitrosyl chloro derivatives.[8]

(18) Piciulo, P. L.; Scheidt, W. R. *Inorg. Nucl. Chem. Lett.* **1975**, *11*, 309 and references therein.

(19) (a) Christodoulou, D.; Wink, D. A.; George, C. F.; Saavedra, J. E.; Keefer, L. K. In *Nitrosamines and Related N-Nitroso Compounds: Chemistry and Biochemistry*; Loeppky, R. N., Michejda, C. J., Eds; ACS Symposium Series 553; American Chemical Society: Washington, DC, 1994; Chapter 25. (b) Christodoulou, D.; Maragos, C. M.; George, C.; Morley, D.; Dunams, T. M.; Wink, D. A.; Keefer, L. K. In *Bioinorganic Chemistry of Copper*; Karlin, K. D., Tyeklár, Z., Eds.; Chapman and Hall: New York, 1993; pp 427−436.

(20) Other *N*-alkylhydroxylaminato groups may also be formed by the reaction of nitric oxide with some transition metal alkyl or aryl complexes:[21,22]



However, reaction of (porphyrin)Fe(R) complexes with NO gas generates the six-coordinate (porphyrin)Fe(NO)R and/or the five-coordinate (porphyrin)Fe(NO).[23]

(21) See chapter 7 in ref 2a for a review NO insertions into metal alkyls.

(22) Bottomley, F. In *Reactions of Coordinated Ligands*; Braterman, P. S., Ed.; Plenum: New York, 1989; Vol. 2, pp 161−167.

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