Theoret. Chim. Acta (Berl.) 60, 379–383 (1981)

THEORETICA CHIMICA ACTA

The Structure of the Active Oxygen Complex of Catalase: Model Calculations

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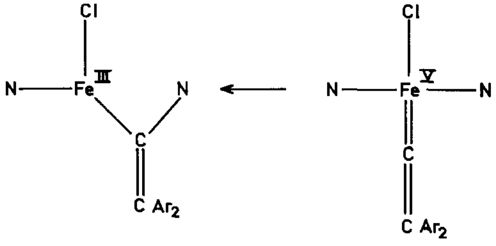
Ab initio SCF calculations are hereafter reported for two stereoisomers of the complex $Fe(N_4C_6H_{10})$ (O) (NH_3), a model of the active oxygen complex of catalase, whose structure is not known. The structure with the oxo ligand in axial position (Fig. 2a) is more stable than the one with the oxygen atom inserted into an iron-nitrogen bond (Fig. 2b) by 33 kcal/mole. Factors that might reduce this difference are discussed.

Key words: Catalase – Iron-Porphyrin – *Ab-initio* SCF Calculations.

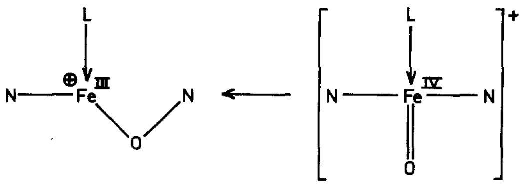
Weiss and Mansuy have recently reported the structure of an iron(III)-porphyrin complex Fe(TTP) $[C=C(p\text{-}ClC_6H_4)_2]Cl$ (**1**) with the vinylidene group inserted into an iron-nitrogen bond as in **1** rather than occupying an axial site as in **2** (scheme I)[1].



1 **2**

Scheme I

They report that complex **1** exhibits a visible spectrum strikingly similar to that of the catalase compound I (CAT I), an intermediate complex obtained by reaction of the hemoprotein catalase with oxidants. An iron(IV) [porphyrin π cation radical] structure such as **4** has been proposed for CAT I. To account for the great similarity of the electronic spectra and magnetic susceptibility of CAT I and complex **1**, Weiss and Mansuy have proposed as an alternative for CAT I a structure such as **3** which is an oxygen analogue of **1**, with the oxygen atom inserted into an Fe(III)—N bond of the heme. They also point out that this type of structure would explain some of the specific reactivities of CAT I [1].



3 **4**

Scheme II

We have investigated theoretically the relative stabilities of the two structures **3** and **4** for a heme model. The model (of formula $N_4C_6H_{10}^{2-}$) which we have used for the porphyrin of the heme is shown in Fig. 1 and has been used previously by us [2, 3] and by others [4]. The models used for the two structures **3** and **4** of CAT I are shown in Fig. 2; we have introduced as the fifth ligand an ammonia molecule to mimic the imidazole ligand which has been found in the resting state of horseradish peroxidase (HRP) [5], a compound closely related to the catalase. We have carried out for the two systems of Fig. 2 both extended Hückel (EHT) and *ab initio* SCF calculations (EHT calculations have also been performed with the porphyrin ligand). The EHT calculations used the standard parameterization for the first-row atoms [6] and the iron parameters were taken from Ref. [7]. The *ab initio* SCF calculations were carried out with the system of programs Asterix [8], using the following basis sets: (13, 8, 6) contracted to [8, 5, 3] for iron [9], (9, 5) contracted to [4, 2] for the first-row atoms [10] and (4) contracted to [2] for hydrogen [11] (the contracted basis set is double-zeta

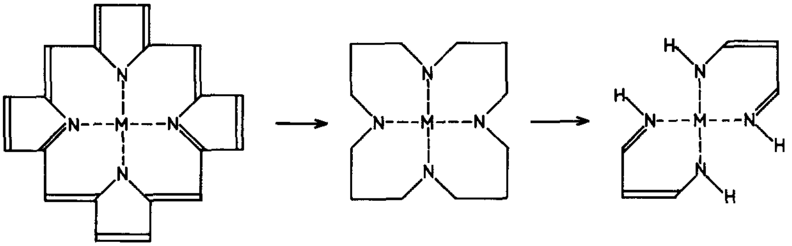


Fig. 1. The metalloporphyrin (left) and the model used (right)

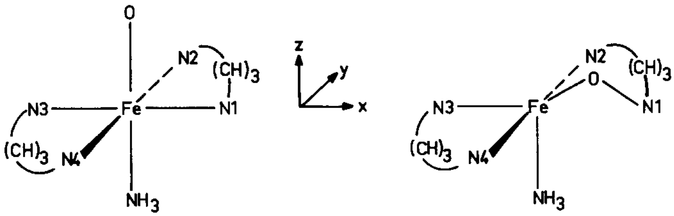


Fig. 2. The models used for the two possible structures of CAT I. Fig. 2a (left) corresponds to structure **4** and Fig. 2b (right) to structure **3**

in general but triple-zeta for the iron 3*d* orbitals and single-zeta for the iron 4*p* orbitals). We have adopted the following geometries:

(1) For the model of Fig. 2a corresponding to structure **4** (axial oxo ligand): Fe—$N_{equat.}$ 1.97 Å, Fe—O 1.65 Å, Fe—N(NH_3) 2.07 Å, C—N 1.38 Å; C—C 1.36 Å, N—H 1.01 Å, C—H 1.08 Å, the iron atom and the two equatorial ligands are in the *xOy* plane. This complex has one plane of symmetry (point group C_s).

(2) For the model of Fig. 2b corresponding to structure **3** (with the O atom inserted into the Fe—N1 bond): the equatorial ligand with the atoms N3 and N4, the atom N2 and the carbon atom α of N2 remain in the *xOy* plane, the iron atom is 0.256 Å below this plane, Fe—N1 2.52 Å, Fe—O 1.73 Å, O—N1 1.24 Å, Fe—N2=Fe—N3=Fe—N4 1.99 Å, the stereochemistry around the N1 atom remains planar and the plane defined by the atoms ON1C1 (C1 being in the α-position of N1) makes an angle of 40° with the *xOy* plane (these parameters have been chosen in analogy with the X-ray structure reported for the vinylidene complex **1** [1]). This system has no element of symmetry (point group C_1).

The ground states are $(39a')^1(21a'')^1\ {}^3A''$ for the complex of Fig. 2a and $(59a)^1(60a)^1\ {}^3A$ for the complex of Fig. 2b. In the former, the iron atom is formally d^4 with an electronic configuration $(xy)^2(xz+yz)^1(xz-yz)^1$ while in the latter it is formally d^6 with a configuration $(xy)^2(yz)^2(xz)^1(x^2-z^2)^1$.

We have reported in Table 1 the *ab initio* SCF energies together with the relative energies of the two structures from the SCF and EHT calculations. Both methods predict that structure **4** should be more stable than structure **3**, the destabilization of structure **3** being nearly one order of magnitude larger in the EHT calculation (205 kcal/mole) than in the SCF calculation (33 kcal/mole). However one will notice that:

– the extremely large destabilization obtained from the EHT calculation is probably not realistic. It has been emphasized that processes in which bond breaking and re-formation occur are on the borderline of what may be reliably treated by this approximate MO method [12]. The reader is referred to Ref. [13] for a more realistic treatment of this type of problem in the EHT approximation. One will notice that for the porphyrin Fe(P)(Cl)(CCH_2) which is closely

Table 1. SCF energies (in a.u.) together with the SCF and EHT relative energies (in kcal/mole) for the two structures of complex $Fe(N_4C_6H_{10})(O)(NH_3)$ and of the porphyrin complexes

		SCF energy	Relative energy	
			SCF	EHT
$Fe(N_4C_6H_{10})(O)(NH_3)$	Structure **4** (Fig. 2a)	−1843.690	0	0
	Structure **3** (Fig. 2b)	−1843.637	33	205
$Fe(P)(O)(NH_3)$[a]	Structure **4**			0
	Structure **3**			237
$Fe(P)(Cl)(CCH_2)$[a]	Structure **2**			0
	Structure **1**			63

[a] P=porphine dianion

related to the system **1** of Weiss and Mansuy, structure **2** is found more stable at the EHT level than structure **1**, a result which is at variance with the experimental structure reported for **1**.

– although the destabilization of 33 kcal/mole for structure **3** at the SCF level appears relatively large, not too much significance should be given to this value since

(1) the value is small enough to be markedly affected by having performed the calculation for a model rather than for the porphyrin.

(2) since we have worked with a model, we have not taken into account the character of a π cation radical of the porphyrin ligand in CAT I. For this reason, our model system has one less open shell than the structures proposed for CAT I.

(3) finally we have relied on assumed geometries for the calculations. Given the highest local symmetry around the iron atom in the structure of Fig. 2a compared to Fig. 2b, it is quite probable that the assumed geometry is a better approximation for the former compared to the latter. This increases probably the destabilization of the structure of Fig. 2b.

For these reasons, we consider still that **3** represents a valuable alternative for the structure of catalase compound I and we are now carrying out the SCF calculations for a model incorporating the porphyrin ligand.

Acknowledgments. We are grateful to Professors R. Weiss and D. Mansuy for helpful discussions and for communicating to us the structure of compound **1** prior to publication.

Note Added in Proof

We have now completed ab initio SCF calculations on the more realistic model system Fe(P)(O) incorporating the porphyrin ligand (A. Strich and A. Veillard, to be published). Structure **4** is now found more stable than structure **3** by

112 kcal/mole, a value much larger than the one of 33 kcal/mole reported in this paper. We ascribe this increased destabilization of structure **3** to the loss of aromaticity of the porphyrin ligand. This value appears large enough to rule out the hypothesis of structure **3** for Compound I of Catalase.

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Received July 21, 1981