# Oxygen Binding to Iron Porphyrins. An ab Initio Calculation

*Sir:*

Studies of synthetic oxygen carriers[1,2] have significantly improved our understanding of the metal-dioxygen linkage in the oxygen carriers oxyhemoglobin and oxymyoglobin. However, a complete understanding of the coordinate link between iron and dioxygen (or carbon monoxide) in the hemoproteins requires further resolution of the following problems.

(i) The alternative description in terms of a Fe(II)-$O_2$ or Fe(III)-$O_2^-$ configuration. Support for the Fe(III)-$O_2^-$ formulation comes from the analogy with the well-documented Co(III)-$O_2^-$ formulation for synthetic oxygen carriers of cobalt,[2] from the behavior in polar solvents of iron(II)-porphyrin complexes,[2] from the ir spectrum of $HbO_2$[3] (but see also ref 1) and from the large quadrupole splittings observed in the Mossbauer resonance spectra of oxyhemoglobin.[4] However, the Fe(III)-$O_2^-$ formulation is ambiguous since it is used to represent both the diradical model of Weiss[5] and $d_\pi$-$p_\pi$ back-bonding from iron to dioxygen in the Pauling model.[6]

(ii) The mode of coordination of molecular oxygen either in an angular, end-on fashion, as first suggested by Pauling[6] and found in the Fe(II) model systems,[1] or in the sideways triangular structure of Griffith,[7] sometimes considered as sterically unfavorable since it would correspond to a formal coordination number of seven,[1] but nevertheless postulated for a dioxygen adduct of a manganese porphyrin.[8]

(iii) The possible stabilization of the coordinated dioxygen through hydrogen bonding to the distal imidazole.[6]

(iv) The nature of the intramolecular motion (rotation about the iron-oxygen bond or inversion at the oxygen atom) interconverting the two types of coordinated dioxygen found in the picket-fence porphyrins[1] and the values of the corresponding energy barriers.

(v) The mode of coordination of carbon monoxide in the carbonyl complexes, either linear (as usually expected) or bent (as proposed for HbCO[9]).

We report here the results of ab initio calculations[10] for the low-spin Fe(II) systems $FePO_2$, $FePO_2(NH_3)$, $FePO_2(NH_3)_2$, and FeP(CO) (P = porphyrin), with the $NH_3$ molecules representing the proximal and distal imidazoles (Im) of hemoglobin and myoglobin.[16] The corresponding energy results are given in Table I. We denote $\pi_g{}^a$ and $\pi_g{}^b$ the two $1\pi_g$ antibonding orbitals of dioxygen, which are degenerate for the free ligand and for a linear structure of the iron-dioxygen unit (for the bent and perpendicular structures the $\pi_g{}^a$ orbital is symmetrical with respect to the $FeO_2$ plane whereas $\pi_g{}^b$ is antisymmetrical). The lowest energy configuration is $(\pi_g{}^a)^2$ for the bent structure but $(\pi_g{}^b)^2$ for the perpendicular structure. These conclusions are similar to the ones which we reached previously for the oxygen adducts of Co(II) complexes.[19] Most important, the perpendicular structure proposed by Griffith turns out to be less stable than the bent one by 55 kcal/mol. Even though this value will change slightly with the theoretical refinements such as the basis set extension and the geometry optimization, the perpendicular structure appears energetically unfavorable for the dioxygen complexes of iron(II) and cobalt(II) porphyrins. However, no premature conclusion should be drawn for the dioxygen adduct of a manganese porphyrin because of the completely different occupations of the 3d orbitals in the high-spin ($S = 5/2$) or intermediate spin ($S = 3/2$) Mn(II) system.[8]

**Table I.** SCF Energies (in au)

| | Electronic configuration | Structure[a] | |
|---|---|---|---|
| $FePO_2$ | $(\pi_g{}^a)^2$ | Bent | −2385.208 |
| | $(\pi_g{}^a)^2$ | Bent[b] | −2385.199 |
| $FePO_2(NH_3)$[c] | $(\pi_g{}^a)^2$ | Bent | −2441.208 |
| | $(\pi_g{}^b)^2$ | Bent | −2441.179 |
| | $(\pi_g{}^a)^2$ | Perpendicular | −2441.020 |
| | $(\pi_g{}^b)^2$ | Perpendicular | −2441.120 |
| $FePO_2(NH_3)_2$ | $(\pi_g{}^a)^2$ | Bent | −2497.117 |
| $FePO_2(NH_3)$ + $NH_3$ | $(\pi_g{}^a)^2$ | Bent | −2497.156 |
| FeP(CO) | $(\pi_g)^0$ | Linear ($\alpha$ = 180°) | −2348.4711 |
| | | Bent ($\alpha$ = 172.5°) | −2348.4702 |
| | | Bent ($\alpha$ = 165°) | −2348.4670 |
| FeP + CO | | | −2348.445 |

[a] With the dioxygen ligand in a plane bisecting the $N_{pyrr}FeN_{pyrr}$ angle unless otherwise stated. [b] With the dioxygen ligand projecting along a $N_{pyrr}FeN_{pyrr}$ axis. [c] Proximal $NH_3$ ligand.

**Table II.** Gross Orbital and Atomic Populations for the Iron and Oxygen Atoms of $FePO_2(NH_3)$ (bent structure)

| | Fe | $O_1$[a] | $O_2$ |
|---|---|---|---|
| s | 6.16 | 3.80 | 3.86 |
| $p_x$, $p_y$ | 4.11 | 1.36 | 1.27 |
| $p_z$ | 4.07 | 1.53 | 1.52 |
| $d_{x^2-y^2}$ | 0.33 | | |
| $d_{xy}$ | 1.91 | | |
| $d_{xz}$, $d_{yz}$ | 1.93 | | |
| $d_{z^2}$ | 0.23 | | |
| Total | 24.78 | 8.05 | 7.93 |

[a] $O_1$ denotes the oxygen atom bound to iron.

Results of the population analysis for $FePO_2(NH_3)$ are reported in Table II. A salient feature is the quasi-neutrality of the dioxygen ligand (contrary to the conclusions of the extended Huckel calculation[18] but in agreement with the results of ab initio GVB-CI calculations for the Fe-$O_2$ unit[22]), thus supporting the description of the iron-dioxygen unit as Fe(II)-$O_2$ rather than Fe(III)-$O_2^-$ (this contrasts with the results of the population analysis for the dioxygen complex of Co(acacen)[17] with a net charge of about 0.5 e on the dioxygen ligand in agreement with a Co(III)-$O_2^-$ formulation). The population of 1.93 for the $d_{xz}$ and $d_{yz}$ orbitals of iron indicates an appreciable $d_\pi$-$p_\pi$ back-bonding from the metal to dioxygen. Again this contrasts with the situation in the dioxygen complex of Co(acacen) with a population close to 2.00 for the $d_\pi$ orbitals (a consequence of the Co(III)-$O_2^-$ configuration unfavorable for back-bonding). These results are in agreement with the experimental finding that the Fe-O bond length of 1.75 Å in the dioxygen complex of the picket-fence porphyrin[1] is appreciably shorter than the Co-O bond length of 1.86 Å in the dioxygen complexes of Co(II), a difference which has been considered as a possible indication of multiple bonding in the Fe(II) complexes. The charge distribution about the iron atom deviates significantly from the symmetric low-spin ferrous configuration $(d_{xy})^2(d_{xz})^2(d_{yz})^2$.

According to Table I, the interaction between the $FeP$-$O_2(NH_3)$ complex and the "distal" ammonia molecule is *repulsive* (the energy of $FePO_2(NH_3)_2$ should be compared to the sum −2497.156 au of the energies of $FePO_2(NH_3)$ and of $NH_3$ calculated with the same basis set, namely −55.948 au). Thus this calculation rules out a possible stabilization of the coordinated dioxygen through hydrogen bonding to the "distal" imidazole (this conclusion is a reasonable one given the quasi-neutrality of the dioxygen ligand). A similar conclusion has been reached on the basis that the "picket fence" porphyrin is a good model for myoglobin but lacks the possibility of hydrogen bonding.[20]

Finally the results of Table I point to: (i) a barrier to the rotation of the dioxygen ligand about the Fe-O bond of 5.6 kcal/mol in $FePO_2$; (ii) a linear structure for the Fe-C-O unit. This latter result is in agreement with a preliminary report of structural analysis for a picket fence carbonyl complex[1] but disagrees with the bent structure proposed on the basis of Mossbauer spectra and extended Huckel calculations.[9] The computed binding energy for the carbonyl ligand is equal to 16 kcal/mol, to be compared to an experimental value of 10 kcal/mol for the binding to deoxymyoglobin.[21]

A more detailed account of this work will be presented elsewhere.[23,24]

**Acknowledgments.** Calculations have been carried out at the Centre de Calcul du C.N.R.S. in Strasbourg-Cronenbourg. We thank the staff of the Centre for their cooperation. This work has been supported through the A.T.P. No. 2240 of the C.N.R.S.

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(10) The LCAO-MO-SCF calculations were carried out with the Asterix system of programs[11] using Gaussian basis sets (10,6,4) for Fe, (7,3) for first-row atoms, and (3) for hydrogen contracted to a minimal basis set (except for the 3d functions which are split). The following geometries were used: for the iron-porphyrin core, the experimental geometry of $\alpha,\beta,\gamma,\delta$-tetraphenylporphinatoiron(II),[12] for the $Fe-O_2$ moiety the experimental values for the dioxygen complex of the "picket-fence" porphyrin,[1] for the "proximal" $NH_3$ ligand the experimental geometry of $NH_3$[13] with an Fe-N bond length of 2.12 Å, for the CO ligand a C-O bond length of 1.16 Å and an Fe-C bond length of 1.77 Å.[14] The nitrogen atom of the "distal" $NH_3$ ligand was positioned according to the x-ray data reported in ref 15. For the perpendicular structure of the $Fe-O_2$ unit we retained the same Fe-O and O-O bond lengths used for the bent structure with the two Fe-O bond lengths equal. The porphyrin plane is the $xOy$ plane with the nitrogen atoms along the $x$ and $y$ axis, the Fe-O axis is the $z$ axis and the O-O axis projects along a bisector of $xOy$.

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(16) This is probably not an unreasonable assumption since a similar calculation for the complex $Co(acacen)ImO_2$ shows no appreciable $\pi$ character in the cobalt-imidazole bond[17]. Extended Huckel calculations for the system $Fe^{II}PO_2Im$ lead to a similar conclusion.[18]

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(24) Note Added in Proof. Similar calculations for the $FePO_2Im$ system yield orbital and atomic populations very close to the ones of Table II for $FeP-O_2(NH_3)$.[23] The two conformations of $FePO_2Im$ with the Fe-O-O plane either parallel or perpendicular to the imidazole plane differ in energy by less than 5 kcal/mol. A double-zeta type calculation for a model-$Fe(N_6C_4H_8)ImO_2$ of the synthetic oxygen carrier of Baldwin and Huff (*J. Am. Chem. Soc.*, **95**, 5757 (1973)) yields conclusions very similar to the above ones (such as the quasi-neutrality of the dioxygen ligand).

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*Received February 2, 1976*

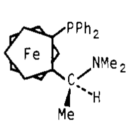
## High Stereoselectivity in Asymmetric Grignard Cross-Coupling Catalyzed by Nickel Complexes of Chiral (Aminoalkylferrocenyl)phosphines

*Sir:*

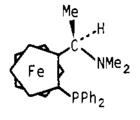
We report here that chiral (aminoalkylferrocenyl)phosphines are effective ligands for the nickel-phosphine catalyzed asymmetric Grignard cross-coupling to form an optically active hydrocarbon, with the aminoalkyl side chain being essential for the high asymmetric induction.

In recent years, catalytic asymmetric reactions have received much attention to obtain chiral molecules efficiently and considerable efforts have been devoted to developing new chiral phosphine ligands.[1,2] Yet, the experimental results so far obtained have told us little about structural features of a ligand which will bring about the highest stereoselectivity in a given reaction.

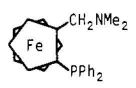
The chiral (aminoalkylferrocenyl)phosphines, which we have recently prepared starting with Ugi's chiral $\alpha$-dimethylaminoethylferrocene[3] and used successfully for the asymmetric hydrosilylation[2] and hydrogenation,[4] are quite unique in that they contain both planar and central elements of chirality, and also an amino group that can interact attractively with an appropriate substrate. These phosphines also offer an advantage over others in permitting one to estimate separately the role which each element of chirality and the functionality plays in an asymmetric reaction by appropriate structural modifications. Thus, (*S*)-$\alpha$-[(*R*)-2-diphenylphosphinoferrocenyl]ethyldimethylamine[2] (PPFA) contains all three features mentioned above, (*S*)-1-dimethylaminomethyl-2-diphenylphosphinoferrocene[5,6] (FcPN) lacks the central chirality, and (*R*)-1-diphenylphosphino-2-ethylferrocene[2] (EPPF) possesses the planar chirality only.



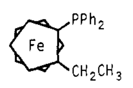
(*S*)-(*R*)-PPFA



(*R*)-(*S*)-PPFA



(*S*)-FcPN



(*R*)-EPPF

Using these chiral phosphines as ligands, the nickel-catalyzed cross-coupling[7] of the 1-phenylethyl Grignard reagent (**1**) with vinyl bromide (**2**) was examined (eq 1). A 1:2 mixture

$$\underset{\mathbf{1}}{\mathrm{PhMeCHMgCl}} + \underset{\mathbf{2}}{\mathrm{CH_2{=}CHBr}} \xrightarrow{[\mathrm{Ni}]^*} \underset{\mathbf{3}}{\mathrm{PhMeC^*HCH{=}CH_2}} \quad (1)$$

of anhydrous $NiCl_2$ and each chiral phosphine was used as a catalyst precursor. The coupling reaction occurred smoothly at −20 to 0° within several hours to give optically active 3-phenyl-1-butene (**3**) in higher than 83% chemical yields. Results summarized in Table I contain three significant features. Firstly, the coupling product of highest optical purity (52-63%) was obtained with PPFA and FcPN. Although the present asymmetric reaction is due to kinetic resolution of the *sec*-alkyl