3098 *Inorg. Chem.* **2010**, *49*, 3098–3100
DOI: 10.1021/ic1001072

Inorganic Chemistry
Communication

Coordination Studies of Bis-Strapped-Hanging-Carboxylate Porphyrins. X-ray Characterization of a Five-Coordinate Iron(II) Complex with a Built-in Axial Base

Ismail Hijazi,[†] Thierry Roisnel,[‡] Marc Fourmigué,[§] Jean Weiss,[⊥] and Bernard Boitrel*,[†]

[†]*ICMV, and* [‡]*CDIFX, and,* [§]*MaCSE, Université de Rennes 1, Sciences Chimiques de Rennes,*
UMR CNRS 6226, 35042 Rennes Cedex, France, and [⊥]*CLAC, UMR CNRS 7177, Université de Strasbourg,*
4 rue Blaise Pascal, 67070 Strasbourg, France

Received January 18, 2010

The comparison of two series of preorganized strapped porphyrins, derived from both the $\alpha\beta\alpha\beta$ and $\alpha\alpha\beta\beta$ conformers of *meso*-tetrakis(aminophenyl)porphyrin, and the coordination studies of their affinity for O_2 are reported. Both series of ligands bear a proximal built-in axial base and a polar distal side defined by either a hanging malonyl ester or a hanging malonic acid residue. In the $\alpha\beta\alpha\beta$ model, the carboxylic acid groups are maintained in an apical location at a fixed distance from the distal oxygen atom of iron-bound O_2. A particular emphasis is placed on the $\alpha\alpha\beta\beta$ series, for which the crystal structure of the five-coordinate ($S = 2$) iron(II) ester complex was determined. In this series, the distal strap can adopt either a tilted conformation or a vertical position over the Fe^{II} core, allowing changes in the distance between the carboxylic groups and the bound O_2.

Biomimetic studies initiated some 30 years ago have led to a better comprehension of O_2 binding in natural hemes and have confirmed Pauling's hypotheses regarding the crucial role of hydrogen bonding in the enhancement of O_2 affinity for a single heme buried in a hydrophobic pocket.[1] The bound O_2 interacts with the histidine residue E7 positioned over the iron atom to establish a hydrogen bond with the superoxo complex (Figure 1).

In various studies, Momenteau et al. compared iron(II) complexes of basket-handle porphyrins, differing only by the nature of the straps (ether or amide). When the straps comprised an amide linkage, one of which incorporated a built-in nitrogen base, the heme model exhibited an O_2 affinity 10 times greater than that for the ether-linked analogue.[2] In a related study using a "picnic-basket" porphyrin possessing amide links, Collman's group reported how the size of the cavity controlled variations in the O_2 binding. Systematic variations of the lengths of the straps connecting the amide anchors in the presence of an exogenic proximal base showed that the smaller the cavity of the picnic basket, the greater the O_2 affinity.[3] In 1995, another systematic variation of a single picket of the picket fence was studied by Reed et al.[4] They reported an interesting 10-fold increase of the O_2 affinity for compounds bearing either a phenylurea-linked picket or a *meta*-phenolamido-linked picket.

Systems bearing appended carboxylic groups were also reported by Chang et al.[5] Starting from a peripheral position of the carboxylic group in a first heme model, this group was relocated to a more apical position by using Kemp's triacid as a spacer. Unfortunately, these interesting models lacked a built-in fifth ligand, and the oxygenated iron complexes proved to be too labile, even at low temperature. More recently, Naruta et al. reported the successful discrimination of CO/O_2 by appending hydroxyl groups on iron twin-coronet porphyrins.[6] Furthermore, electron paramagnetic resonance techniques were used in the case of dipolar hydrogen-bond donation from a hanging imidazole to demonstrate the interaction with O_2 bound to a cobalt porphyrin model.[7]

In this work, attention was focused on the possible influence of carboxylic acids hanging over the O_2 coordination site in two series of synthetic O_2 carriers that mainly differ by the flexibility of their straps. Both models in Figure 1 incorporate a malonic acid held above the sixth coordination site by a rigid, yet flexible strap. The $\alpha\beta\alpha\beta$ series of models **2a**, bearing an ethyl malonyl ester, and **2b** were synthesized by a steric decompression method and led to the expected five-coordinate complexes.[8] Porphyrin **1a** was obtained either directly

---

*To whom correspondence should be addressed. E-mail: bernard.boitrel@univ-rennes1.fr.

(1) Pauling, L.; Weiss, J. J. *Nature* **1964**, *203*, 182–183.

(2) (a) Momenteau, M.; Mispelter, J.; Loock, B.; Lhoste, J.-M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 61–70. (b) Momenteau, M.; Mispelter, J.; Loock, B.; Lhoste, J.-M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 221–231. (c) Momenteau, M.; Loock, B.; Huel, C.; Lhoste, J.-M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 283–295.

(3) Collman, J. P.; Zhang, X. M.; Wong, K.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 6245–6251.

(4) Wuenschell, G. E.; Tetreau, C.; Lavalette, D.; Reed, C. A. *J. Am. Chem. Soc.* **1992**, *114*, 3346–3355.

(5) Chang, C. K.; Liang, Y.; Aviles, G.; Peng, S.-M. *J. Am. Chem. Soc.* **1995**, *117*, 4191–4192.

(6) Tani, F.; Matsu-ura, M.; Ariyama, K.; Setoyama, T.; Shimada, T.; Kobayashi, S.; Hayashi, T.; Matsuo, T.; Hisaeda, Y.; Naruta, Y. *Chem.—Eur. J.* **2003**, *9*, 862–870.

(7) Dube, H.; Kasumaj, B.; Calle, C.; Saito, M.; Jeschke, G.; Diederich, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 2600–2603.

(8) Balieu, S.; Hijazi, I.; Motreff, N.; Lachaud, F.; Even-Hernandez, P.; Boitrel, B. *Org. Lett.* **2010**, *12*, 8–11.

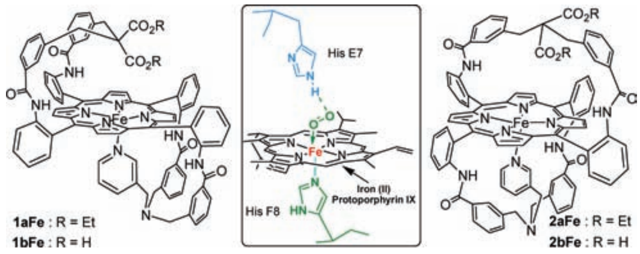
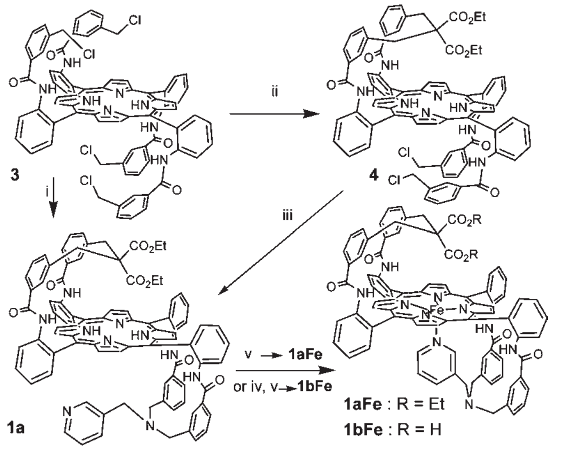


Figure 1. Myoglobin coordination site (center) and appended-carboxylate or ethyl ester porphyrins in two different conformations: $\alpha\alpha\beta\beta$ (left) and $\alpha\beta\alpha\beta$ (right).

Scheme 1. Synthesis of Porphyrins **1a** and **1b**[a]



[a] (i) diethylmalonate, EtONa, *C*-pyridin-3-ylmethylamine, THF, 12 h, 80 °C (10%); (ii) diethylmalonate, EtONa, CH_2Cl_2 (60%); (iii) *C*-pyridin-3-yl-methylamine, NaI, K_2CO_3, THF, 3 days (85%); (iv) BBr_3, CH_2Cl_2, room temperature, overnight (56%); (v) glovebox, < 2 ppm O_2, $FeBr_2$, reflux THF, overnight.

from porphyrin **3**[9] (Scheme 1) or more efficiently starting with the formation of the diethylmalonato single-strapped porphyrin **4**, followed by the incorporation of *C*-pyridin-3-ylmethylamine. In both series, subsequent hydrolysis affords the carboxylic acid group. Previously reported X-ray structures as well as ^{1}H NMR studies of structural analogues clearly established that the distal straps of models **1** and **2** can adopt various conformations, allowing variation of the location of the carboxylic groups.[10]

In model **2b**, the carboxylic group can only change its location by rotation of the strap around the axis of the 5 and 15 meso positions; the distance between the carboxylic group and the iron atom remains invariable. In **1b**, the carboxylic group has a restricted degree of freedom because of anchoring of the strap at the 5 and 10 meso positions. This restriction offers a higher degree of control over the position of the hydrogen-bond donor group but a variable distance from the Fe^{II} core. Whereas no rotation is possible around the 5 and 10 meso positions, the only change in the carboxylic group's location arises from bond rotations around the benzylic carbon atoms in the strap. Consequently, the coordination chemistry of these models is well-controlled and should lead to stable O_2 adducts with similar, yet different behaviors.

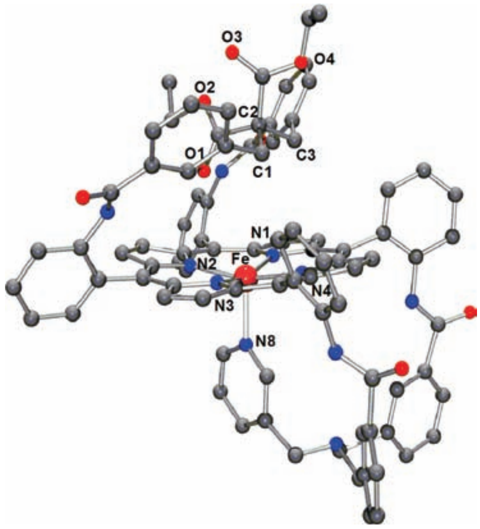


Figure 2. X-ray structure of five-coordinate ferrous complex $\mathbf{1aFe^{II}}$.

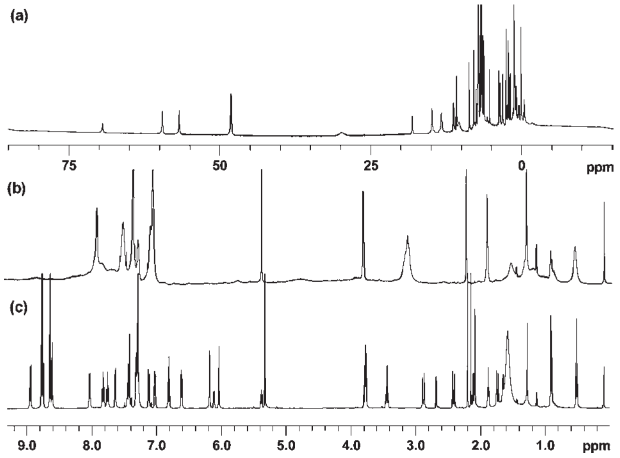


Figure 3. ^{1}H NMR spectra (500 MHz, $CDCl_3$, 313 K) of (a) $\mathbf{1aFe^{II}}$; (b) part a + O_2; (c): part b + CO.

Insertion of iron into porphyrin **1a** yielded the five-coordinate complex $\mathbf{1aFe^{II}}$. This complex exhibits a ^{1}H NMR spectrum that is typical of a paramagnetic ($S = 2$) complex (Figure 3a), establishing that the built-in axial ligand is coordinated to the iron. Moreover, the crystallographic structure of model $\mathbf{1aFe^{II}}$, represented in Figure 2, confirms this coordination sphere. X-ray structures of such five-coordinate ferrous hemes containing a single axial base are rather scarce.[11] Only one example with a built-in nitrogen

---

[9] Halime, Z.; Balieu, S.; Lachkar, M.; Roisnel, T.; Richard, P.; Boitrel, B. *Eur. J. Org. Chem.* **2006**, 1207–1215.

[10] (a) Halime, Z.; Lachkar, M.; Roisnel, T.; Furet, E.; Halet, J.-F.; Boitrel, B. *Angew. Chem., Int. Ed.* **2007**, *46*, 5120–5124. (b) Halime, Z.; Lachkar, M.; Roisnel, T.; Richard, P.; Boitrel, B. *Inorg. Chem.* **2007**, *46*, 6338–6346.

[11] (a) Jameson, G. B.; Rodley, G. A.; Robinson, W. T.; Gagne, R. R.; Reed, C. A.; Collman, J. P. *Inorg. Chem.* **1978**, *17*, 850–857. (b) Jameson, G. B.; Molinaro, F. S.; Ibers, J. A.; Collman, J. P.; Brauman, J. I.; Rose, E.; Suslick, K. S. *J. Am. Chem. Soc.* **1980**, *102*, 3224–3237. (c) Rodgers, S. J.; Koch, C. A.; Tate, J. R.; Reed, C. A.; Eigenbrot, C. W.; Scheidt, W. R. *Inorg. Chem.* **1987**, *26*, 3647–3649. (d) Momenteau, M.; Scheidt, W. R.; Eigenbrot, C. W.; Reed, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 1207–1215. (e) Mandon, D.; Ott-Woelfel, F.; Fischer, J.; Weiss, R.; Bill, E.; Trautwein, A. X. *Inorg. Chem.* **1990**, *29*, 2442–2447. (f) Ellison, M. K.; Schulz, C. E.; Scheidt, W. R. *Inorg. Chem.* **2002**, *41*, 2173–2181. (g) Hu, C.; Noll, B. C.; Schulz, C. E.; Scheidt, W. R. *Inorg. Chem.* **2005**, *44*, 4346–4358. (h) Hu, C.; Noll, B. C.; Schulz, C. E.; Scheidt, W. R. *J. Am. Chem. Soc.* **2005**, *127*, 15018–15019. (i) Hu, C.; An, J.; Noll, B. C.; Schulz, C. E.; Scheidt, W. R. *Inorg. Chem.* **2006**, *45*, 4177–4185.

Table 1. O_2 Binding Constants (Benzene, 25 °C)

	$\mathbf{1aFe^{II}}$	$\mathbf{1bFe^{II}}$	$\mathbf{2aFe^{II}}$	$\mathbf{2bFe^{II}}$
$P_{1/2}$ (Torr)	1	nonmeasurable	10^{-1}	10^{-3}

base has been reported by Karlin et al.[12] This unique example was obtained for a cytochrome *c* oxidase model in which a 2-pyridyl arm of the Cu_B chelate migrated to the iron center located 0.420 Å out of the mean 24-atom porphyrin plane toward the pyridyl axial base. Whereas crystals of Karlin et al.'s five-coordinate complex were obtained at −15 °C, those of $\mathbf{1aFe^{II}}$ were grown at room temperature in a glovebox. The fifth ligand, composed of a *C*-pyridin-3-ylmethylamino arm, pulls the iron atom 0.430 Å out from the mean 24-atom porphyrin plane.

This value compares very well with Karlin et al.'s model discussed previously (0.420 Å). The $Fe-N_{py}$ bond length is 2.169 Å, which is slightly longer than that in the structure of Collman's picket-fence complex containing an imidazole axial ligand[13] (2.070 Å) but shorter than that in Karlin et al.'s model with a pyridine axial ligand (2.229 Å). This bond length is consistent with some constraints in the coordination of the fifth ligand. The coordination of the proximal built-in base exerts a compression motion on the two amides that anchor the strap to the meso aromatic substituents.

Consequently, both *meso*-phenyls are displaced toward the distal side (Figure 2) to accommodate the pyridine binding. A final clue for the constrained binding of the proximal base is the 7° deviation from the normal to the porphyrin's mean plane. The distal strap in $\mathbf{1aFe^{II}}$ is bent over the free coordination site of the iron, with an angle to the mean plane of the porphyrin of about 45°, positioning the closest carboxyl oxygen atom at a short distance of 3.589 Å from the center of the porphyrin.

O_2 binding was monitored by both ^1H NMR and UV−vis spectroscopies. Affinities were calculated by classical methods (Table 1; see pp S3 and S4 in the Supporting Information for a detailed method). It is worth mentioning that the O_2 adducts were stable in solution over a period of several weeks. In the $\alpha\beta\alpha\beta$ series, the $P_{1/2}(O_2)$ values were 10^{-1} Torr for the ester compound $\mathbf{2aFe^{II}}$ and 10^{-3} Torr for the acidic complex $\mathbf{2bFe^{II}}$ (Table 1). The increase in the affinity for the acidic compound is consistent with that of a hydrogen bond between the hanging carboxylic group and the bound superoxo, which leads to a O_2 affinity comparable to that of oxygen-avid hemoglobin of Ascaris.[14]

In the $\alpha\alpha\beta\beta$ series, $\mathbf{1aFe^{II}}$ exhibited $P_{1/2} = 1$ Torr, which was an order of magnitude smaller than that of its $\alpha\beta\alpha\beta$ counterpart. The rationale for this result could be that the coordination site of $\mathbf{1aFe^{II}}$ is less accessible than that in $\mathbf{2aFe^{II}}$, in which the distal strap is bent over the free coordination position (Figure 2). Exposure of this paramagnetic five-coordinate complex $\mathbf{1aFe^{II}}$ (Figure 3a) to an oxygen atmosphere yielded a diamagnetic complex (Figure 3b). Although the NMR spectrum of $\mathbf{1aFe^{II}\text{-}O_2}$ is not well-resolved, impurities and/or oxidation could be ruled out, as shown by the NMR signature of $\mathbf{1aFe^{II}\text{-}CO}$. The latter was obtained by the direct bubbling of CO into a solution of $\mathbf{1aFe^{II}\text{-}O_2}$, 72 h after the formation of $\mathbf{1aFe^{II}\text{-}O_2}$ (Figure 3c). This NMR spectrum is perfectly diamagnetic and very well-resolved, which demonstrates that the O_2 adduct was not oxidized. Presumably, the poor resolution of the NMR spectrum of $\mathbf{1aFe^{II}\text{-}O_2}$ can be attributed to exchange processes on the NMR time scale and/or some privileged orientations of the superoxo complex relative to the distal strap.

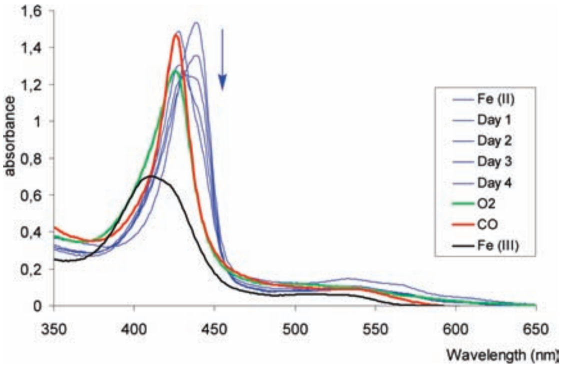


Figure 4. UV−vis monitoring of O_2 and CO binding to $\mathbf{1bFe^{II}}$ (benzene).

For the acidic complex $\mathbf{1bFe^{II}}$, the starting compound did not exhibit a typical five-coordinate UV−vis spectrum. Indeed, without the addition of O_2, the Soret absorption shifted from 440 to 428 nm over a period of 4 days (Figure 4). However, the same sample still binds O_2 (green curve) and further binds CO (red curve), ruling out any oxidation. In light of the X-ray structure of its precursor $\mathbf{1aFe^{II}}$, it is possible that in $\mathbf{1bFe^{II}}$ either a water molecule, stabilized by hydrogen bonding with one of the carboxylic groups,[15] or one of the carboxylic groups itself is bound to the iron atom. This peculiar behavior explains why the $P_{1/2}$ evaluation (Table 1) was not possible; however, these hypotheses need to be investigated.

This study indicated that various iron(II) models delivering a carboxylic group in an almost apical position relative to the center of the porphyrin not only exhibited a high O_2 affinity but also remained unoxidized after several weeks. The structural data clearly indicate that the spatial location of the carboxylic groups encountered in our models is adequate for hydrogen bonding with the superoxo complex. Work is in progress to further characterize these complexes in the solid state.

Acknowledgment. This work was supported by the CHEMBLAST program (Grant BLAN 0230) of the National Research Agency and Région Bretagne.

Supporting Information Available: Syntheses, O_2 titrations, and spectroscopic and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data have also been deposited with the Cambridge Crystallographic Centre as supplementary publication CCDC 761839. The coordinates can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K. (e-mail: deposit@ccdc.ca-m.ac.uk).

---

(12) Kim, E.; Helton, M. E.; Lu, S.; Moenne Loccoz, P.; Incarvito, C. D.; Rheingold, A. L.; Kaderli, S.; Zuberbuhler, A. D.; Karlin, K. D. *Inorg. Chem.* **2005**, *44*, 7014–7029.

(13) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Robinson, W. T.; Rodley, G. A. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 1326–1329.

(14) Golberg, D. E. *Chem. Rev.* **1999**, *99*, 3371–3378.

(15) Collman, J. P.; Decréau, R. A.; Dey, A.; Yang, Y. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 4101–4105.