Equilibrium O$_2$ and CO binding behaviour of two dendritic iron(ii) porphyrin systems is reported.

Tetrameric haemoglobin (Hb) and monomeric myoglobin (Mb) are haem proteins responsible for dioxygen storage and transport in biological systems. In the deoxy forms of both Hb and Mb the haem iron is bound to a single, ‘proximal’, axial imidazole resulting in a five-coordinate high-spin (S = 2) Fe$^{III}$; upon oxygenation at the opposite ‘distal’ face, a diamagnetic Fe$^{III}$O$_2$– complex forms reversibly. The protein superstructure is responsible for the kinetic stabilization of the oxygenated form; amino acid residues on the ‘distal’ porphyrin face appear to destabilize a competing complex derived from the endogenous toxic CO. Thus the ‘M’ value (i.e. the ratio of the two equilibrium binding constants $K_{CO}/K_{O2}$) for Hb and Mb is about 100, small enough that the body can tolerate low, endogenous levels of CO. The ‘picket fence’ iron(ii) model† complex also binds O$_2$ reversibly, exhibiting an O$_2$ affinity about the same as that of Mb; the polar O$_2$ binding cavity kinetically stabilizes the intrinsically bent O$_2$ adduct. In contrast, the linear CO ligand binds very strongly to the ‘picket fence’ porphyrin; M for the T (tense)-state model is 4820,1 Several subsequent model systems such as ‘pocket’,2 ‘hybrid’,3 and ‘capped’4 porphyrins effect some distortion of the CO ligand and, as a consequence, M is lowered to ca. 150; with more hindered cavities, M can fall below 1.5 The detailed interaction between structural distortion and equilibrium affinities of CO remains controversial.5

Stabilization of bound O$_2$ is also poorly understood. A distal histidine residue in Hb and Mb forms a weak [stability ca. 2 kcal mol$^{-1}$ (1 cal = 4.184 J)] hydrogen bond to the terminal oxygen in the Fe$^{III}$O$_2$– adduct. There have been some attempts to imitate such a hydrogen bond with model iron(ii) porphyrins.7 Some haem proteins have an unusually high O$_2$ affinity; for example in the blood worm Ascaris,8 the O$_2$ affinity is 10$^3$-fold higher compared with Mb. One can speculate that a strong hydrogen bond is responsible for this high O$_2$ affinity.

With the recent surge in dendrimer technology,9 dendritic porphyrins were prepared as synthetic models of globular haem proteins.10,11 It was shown for aqueous solutions that, in analogy to the protein surroundings in electron transfer proteins, a densely packed dendritic shell around a deeply buried iron haem profoundly influences the redox potential of the bioologically relevant Fe$^{III}$–Fe$^{II}$ couple.$^{10b}$ Recently, Jiang and Aida$^{11b}$ reported a dendritic iron(ii) porphyrin with aryl ether branches which exhibits reversible dioxygen binding. However, in their study, a 1-methylimidazole was used. This ligand is known to form a six-coordinate, low-spin iron(ii) complex. This factor complicates any measure of O$_2$ affinity.

Herein we report a gas equilibrium binding study with two dendritic iron(ii) porphyrins of first (G1-Fe$^{II}$, $M_r$ = 3956) and second (G2-Fe$^{II}$, $M_r$ = 11296) dendritic generation (Fig. 1). These were prepared from the corresponding free-base dendritic porphyrins$^{10b}$ via metallation with FeBr$_3$ in THF in an inert atmosphere box and subsequently purified chromatographically (SiO$_2$, MeOH–CH$_2$Cl$_2$).‡ The dendritic iron(ii) porphyrins were each dissolved in toluene, 1000 mol equiv. of 1,2-dimethylimidazole (dimim) were added to form the five-coordinate, high-spin iron(ii) complex, and the solution was loaded into a tonometer for gas binding studies. The dmim ligand forms only a 1:1 high-spin iron(ii) adduct obviating the problem of controlling the number of axial ligands. Furthermore, the corresponding iron(iii) porphyrin is a good model for the lower affinity T-state of Hb.12

Gas flow: O$_2$, then N$_2$, then O$_2$ UV–VIS experiments showed reversible O$_2$ binding in toluene solution at 25 °C. Using a tonometer, we measured the O$_2$ and CO equilibrium binding constants ($K_{O2}$ and $K_{CO}$) for both dendrimers G1-Fe$^{II}$ and G2-Fe$^{II}$. These $P_{1/2}(O_2)$ ($= 1/K_{O2}$) and $P_{1/2}(CO)$ ($= 1/K_{CO}$) values are displayed in Table 1 compared with those of T-state Hb, the corresponding T-state ‘picket fence’ model, and of the blood worm Ascaris.

It is remarkable that the O$_2$ affinities [$K_{O2}$ = 1/$P_{1/2}(O_2)$] of the dendritic porphyrins are about 1500 times greater than those of T-state Hb; these values approach the high affinity of Ascaris (Table 1). The CO affinities of the dendritic porphyrins are lower than those of the ‘picket fence’ model but are close to the value of Hb in the T-state. The combination of high O$_2$ and low

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**Fig. 1** Dendritic porphyrins G1-Fe$^{II}$ and G2-Fe$^{II}$
Values show a trend similar to G2-Fe II /dmim activities. The measured O2 affinities are about 1500 times porphyrin, implying a possible hydrogen bonding between the terminal O of bound O2 and the NH of the amide group linking together the porphyrin core and the first-generation dendritic branches, suggesting that the terminal O of bound O2 can form such a hydrogen bond with the NH of the amide group linking together the porphyrin core and the first-generation dendritic branches, but more evidence is needed; studies are in progress. The lower CO affinity, the dendritic model systems are more like Hb than Hb (T-state).

Changing solvent polarity may slightly affect the affinities. 15

Ascaris.

Table 1 Oxygen and carbon monoxide binding data

<table>
<thead>
<tr>
<th></th>
<th>P_{1/2}(O2)/1/2 (Torr)</th>
<th>P_{1/2}(O2)/</th>
<th>P_{1/2}(CO)/</th>
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<tbody>
<tr>
<td>O2</td>
<td></td>
<td>M</td>
<td></td>
</tr>
<tr>
<td>CO</td>
<td></td>
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<tr>
<td>Hb (T-state)</td>
<td>40</td>
<td>0.30</td>
<td>135</td>
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<tr>
<td>Fe (picket fence)/dmim</td>
<td>38</td>
<td>0.0089</td>
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<td>Ascaris</td>
<td>0.002</td>
<td>0.1</td>
<td>0.02</td>
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<td>G1-FeII/dmim</td>
<td>0.035</td>
<td>0.35</td>
<td>0.10</td>
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<tr>
<td>G2-FeII/dmim</td>
<td>0.016</td>
<td>0.19</td>
<td>0.08</td>
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</table>

Conditions: *H2O, pH 7, 25 °C.*  *Toluene, 25 °C.*  *H2O, pH 7, 20 °C.*  Changing solvent polarity may slightly affect the affinities. 15

In conclusion, we have studied two dendrimer-based myoglobin T-state models. Each exhibits reversible O2 and CO binding activities. The measured O2 affinities are about 1500 times higher than those of a haemoglobin and 'picket fence' porphyrin, implying a possible hydrogen bonding between the terminal O of bound O2 and an amide N–H group. In terms of CO affinity, the dendritic model systems are more like Hb than uncapped haem (e.g. 'picket fence' porphyrin) suggesting that, as with Hb, bound CO experiences a steric interaction that distorts binding from a favourable linear conformation.

Footnotes


2 UV–VIS spectra in toluene of G1-FeIII: λmax (ε) = 428 nm (4.1 × 105 m–1 cm–1); and G2-FeIII: λmax (ε) = 408 nm (2.2 × 105 m–1 cm–1).

References


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