Co-operative Ligation of Diporphinatoiron(ii) Complexes with Carbon Monoxide: a Haemoglobin Model for Gaseous Molecule Ligation

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Carbon monoxide ligation to diporphinatoiron complexes is demonstrated with kinetic and equilibrium measurements: the diporphinatodi-iron–imidazole complex shows strong co-operativity in the ligation.

The nature of co-operativity in haemoglobin (Hb) ligation with oxygen (O_2) or carbon monoxide (CO) is thought to be a result of the four porphinatoirons forming an integral part of the same conformational system.[1,2] Several attempts have been reported to mimic the co-operative ligation of Hb by the use of porphinatoiron in solid state,[3] porphinatoiron attached to a polymer,[4] and dimeric porphinato-iron[5] and -cobalt.[6] In the present work, we synthesized diporphinatodi-iron (1a), diporphinatoiron–copper (1b), and diporphinatoiron–metal free (1c), and the CO-ligation to them was studied with kinetic and equilibrium data: (1a) showed a strong co-operativity in the ligation.

Using a modification of the method described in refs. 7—9 we prepared iron(ii) complexes of (1) and 3,8,13,18-tetramethyl-1,17-diethylporphin 2,12-diacetic acid dimethyl ester (2); with 1-methylimidazole in benzene solution, $\lambda_{max.}$: (1a), 412 and 554 nm; (1b), 395 and 568 nm; (1c), 411 and 555 nm; (2), 412, 520, and 553 nm. Molar absorption coefficients per Fe ion were equivalent for (1a)—(1c). The double peak visible absorption spectrum of (2) with 1-methylimidazole is assigned to a hexaco-ordinate porphinatoiron(ii) complex. On the other hand, the visible spectra of (1a)—(1c) with 1-methylimidazole are characterized by a single peak absorption, which is assigned to a pentaco-ordinate structure. This means that the imidazole ligand co-ordinates to the Fe of (1) only from the outward-facing side owing to the steric structure of the diporphyrin. That is, only small gaseous molecules can ligate to the Fe from the inner-facing side of the porphyrin.

The absorbances of the (1)–CO complexes were $\varepsilon = 2.74 \times 10^5$ dm^3 mol^{-1} cm^{-1} ($\lambda_{max.}$; 411 nm) and 2.8×10^4 (538) for (1a) and $\varepsilon = 1.43 \times 10^5$ dm^3 mol^{-1} cm^{-1} ($\lambda_{max.}$; 411 nm) and 1.5×10^4 (535) for (1b) and (1c). The ε value for (1a) being twice that of (1b) or (1c) implies that two CO molecules bind with one (1a) molecule owing to the di-iron structure.

The CO-ligation rate constants (k_{on} and k_{off}) were measured by flash-photolysis (Table 1). The time–reaction curves for the CO-ligation to (1) and (2) after photodissociation of the CO complexes could be approximated by mono-phase kinetics within experimental error. The time–reaction curve for the CO-ligation of (1a), having two ligation-sites in

one molecule, was also mono-phase. The k_{on} values of (1b) and (1c) were 10^4 times smaller than that of the non-capped (2) and chelated haem[10] probably owing to the steric effect of the diporphyrin structure. The k_{on} value for (1a) was further reduced in comparison with those of (1b) and (1c).

CO-ligation equilibrium curves for (1) were measured using a CO titration method[11] and are shown in Figure 1. The CO pressure at half CO-ligation ($p_{1/2}$) is given in Table 1. The $p_{1/2}$ values of (1a)—(1c) are close to those of Hb, Mb, and diporphinatoiron–copper[7] but not that of (2). The $p_{1/2}$ value of (1a) is 2—5 times larger than those of (1b) and (1c) although (1a)—(1c) have the same sterically hindered structure. This corresponds to the smaller k_{on} value of (1a) in comparison with (1c).

Figure 1 demonstrates that the CO-ligation equilibrium curve for (1a) appears sigmoidal while the curves for (1b) and (1c) are hyperbolic. Co-operative parameters (n)[12] were estimated from the Hill plot[12] for the CO-ligation to (1a) to be 3.4 which meant a strong co-operativity occurred in the ligation, while those for (1b) and (1c) were unity (n for Hb = 2.8, Mb = 1.0).

This co-operative CO-ligation phenomenon may be explained by the following porphinatoiron–porphinatoiron interaction. Planar porphinatoirons of (1a) are linked
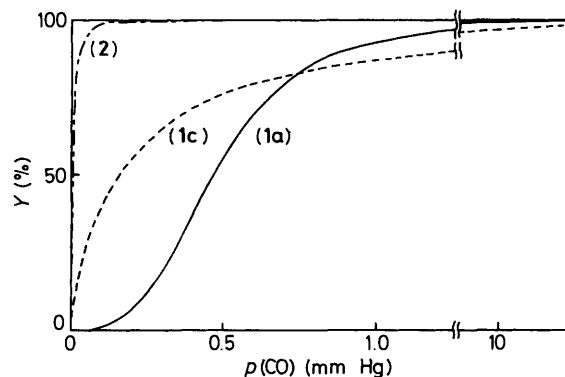

Figure 1. CO-binding and -dissociation equilibrium curves of the diporphinatometal complexes in benzene at 20 °C.

Table 1. CO-binding rate parameters and CO-binding affinity of the diporphinatometal complexes in benzene at 20 °C.

Haem	Solvent	k_{on} (dm^3 mol^{-1} s^{-1})	k_{off} (s^{-1})	$p_{1/2}$ (mm Hg)
(1a)/1-MeIm[a]	Benzene	6.0×10^2	0.0050	0.47
(1b)/1-MeIm	Benzene	5.4×10^4	0.056	0.10
(1c)/1-MeIm	Benzene	4.6×10^4	0.076	0.16
(2)/1,2-Me$_2$Im[b]	Benzene	2.8×10^8	5.8	0.0020
Chelated haem[c]	H$_2$O (pH 7)	3.6×10^6	0.0089	—
Haemoglobin[d]	H$_2$O (pH 7)	1.0×10^5	0.090	0.087
Myoglobin (Mb)[d]	H$_2$O (pH 7)	5.0×10^5	0.017	0.0033

[a] 1-MeIm = 1-methylimidazole. [b] 1,2-Me$_2$Im = 1,2-dimethylimidazole. [c] From ref. 10. [d] From ref. 1.
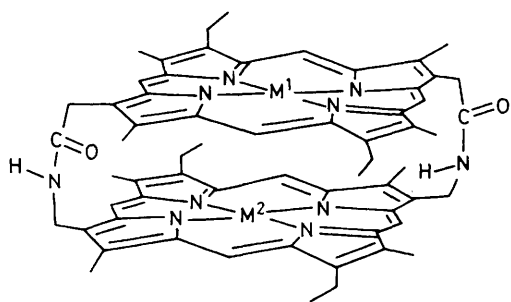
(1)

a;	M^1 = Fe,	M^2 = Fe
b;	M^1 = Cu,	M^2 = Fe
c;	M^1 = Fe,	M^2 = H$_2$
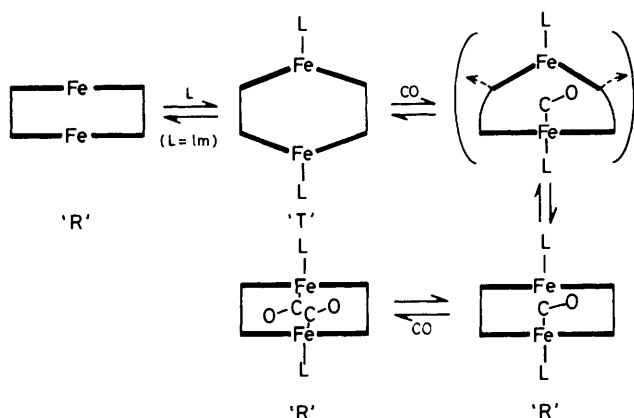
Scheme 1. Co-operative CO-ligation profile of the diporphinatodi-iron complex.

covalently with rigid amido bond-bridges in a parallel and stable face-to-face structure [probably corresponding to the 'relaxed (R)' state of Hb, see Scheme 1]. For (1a) two imidazole ligands co-ordinate to the porphinatoiron only from the outward-facing side. This leads to the pentaco-ordinate, high-spin porphinato iron complex where the Fe ions lie slightly out of the plane and the porphyrin planes are distorted [probably corresponding to the 'tense (T)' state of Hb]. When one of the porphinatoiron–imidazole complexes of (1a) ligates with CO, the 'T' structure changes to that of the hexaco-ordinate, low-spin CO complex, and then the porphyrin plane ligated with CO becomes strictly planar. This structural change of the first ligated porphinatoiron induces the facing, distorted porphyrin to return the planar 'R' state, which facilitates the CO ligation to this second porphinatoiron.

A similar co-operative ligation of (1a) was observed with oxygen in cooled benzene but a quantative result was not given owing to the short life-time of the (1a)–oxygen adduct.

The co-operative ligation of synthetic (1a) with gaseous molecules is produced by structural changes of the coupled ligation-sites (porphinatoirons) and is a good model of the co-operative ligation of Hb where conformational change of the globin protein induces the reactivity change of porphinato-iron.

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