'Jellyfish' Type Cobalt(II)porphyrins as a Hemoprotein Model and their Regulated Dioxygen Affinities by Steric Restrictions on Axial Ligands

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The stereo-regulation for the dioxygen affinities of hemoproteins could be divided into two main parts: distal histidine site (cavity) and proximal histidine site. It is widely accepted that the dioxygen affinity of the T-structure in the α subunits of hemoglobin (Hb) is lowered mostly by the tilt of the proximal histidine relative to the heme which opposes its movement toward the porphyrin plane [1]. Nevertheless, there have been few reports on the effects of binding modes (bond angle, bond length, etc.) of axial ligands on the dioxygen affinities [2–4]. Here, to examine the effect of the orientation of axial ligands on the dioxygen affinities, so-called 'jellyfish' type porphyrinatocobalt(II) complexes were designed and synthesized, in which the orientation of the plane of the axial ligands could be controlled by steric restrictions in the molecule.

'Jellyfish' porphyrin **IIIa** (Fig. 1) was derived from the coupling with 5α,10β,15α,20β-tetra(2-aminophenyl)porphyrin and nonanedioyl dichloride, followed by treatment with pivaloyl chloride. **IIa** and **IVa** were prepared by the known method [5]. **Ia** was prepared by the diazotization of 5α,15α-bis(2-aminophenyl)-10β,20β-(2,2′-heptamethylene-1,9-dicarbonylaminophenyl)porphyrin, followed by the eliminitation of diazonium groups by hypophosphorous acid. Cobalt(II) insertion to the porphyrins was carried out by the $CoCl_2$–THF method** [5].

In the 'jellyfish' porphyrinatocobalt(II) complexes **IIb** and **IIIb**, valeryl groups or pivaloyl groups were appended on one side of the porphyrin plane in order to control the orientation of an axial ligand such as 1-methylimidazole (1-MeIm), and the ligand binding to the other side of the porphyrin plane was inhibited by constructing a 'strapped' structure [5]. In complex **Ib**, since the same 'strapped' structure was introduced into one side of the porphyrin plane, there were no appended substituents on the other side. Therefore, no steric restriction might be imposed on the axial ligand binding to **Ib**.

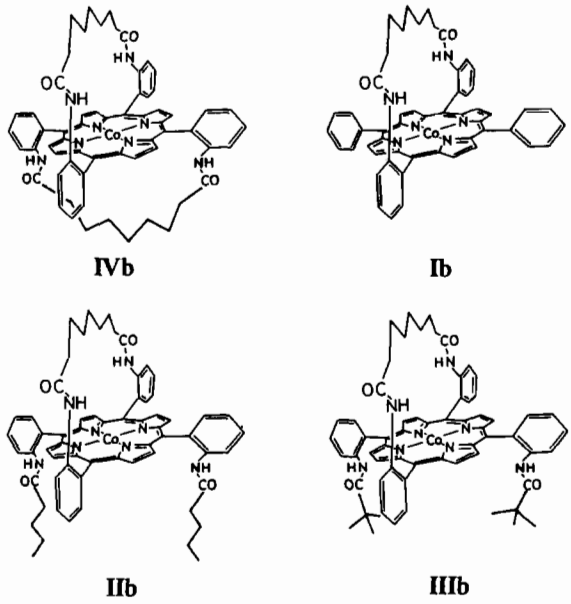

Fig. 1. 'Jellyfish' type porphyrinatocobalt(II) complexes. Free base porphyrins of **Ib**, **IIb**, **IIIb** and **IVb** are represented as **Ia**, **IIa**, **IIIa** and **IVa** respectively.

The dioxygen affinities and the K_B values were determined by means of spectrophotometric titrations in toluene at 25 °C [5] (Table 1). On the axial ligand binding, the small K_B value for complex **IVb** means that the 1-MeIm binding to the side of the porphyrin plane having the strapped structure is inhibited selectively and that the binding takes place on the other side of the porphyrin plane. The K_B values increase with the bulkiness of appended substituents on the ligand binding site. These results are explained by considering that for the axial ligand bindings these substituents perform the same function that a cavity does for dioxygen bindings; that is, a more bulky substituent constructs a more effective cavity and consequently enhances the axial ligand bindings.

In contrast, the dioxygen affinities of 'jellyfish' porphyrinatocobalt(II) complexes decrease with increasing bulkiness of the appended substituents. This phenomenon is very interesting, because these complexes have the same cavity which affects mainly the dioxygen affinities in model compounds as well as hemoproteins. Here, it may be reasonable that these differences are attributed to the changes in stereochemical environments at the binding sites for 1-MeIm. It is well known that the dioxygen affinities of porphyrinatocobalt(II) increase with increasing σ- and π-electron donations of an axial ligand [7, 8]. While the former is independent of the orientation

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**Abbreviations: THF, tetrahydrofuran; $P_{1/2}O_2$. half-saturation pressures of dioxygen for dioxygen binding; α^2-*trans*-TPivPP, 5α,10β,15α,20β-tetrakis(o-pivalamidophenyl)-porphyrin dianion.

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TABLE I. Axial Ligand and Dioxygen Bindings to 'Jellyfish' Porphyrinatocobalt(II) Complexes[a]

Complex	K_B[b] (M^{-1})	$P_{1/2}$[c] (torr)
IVb	1.1×10^2	—[d]
Ib	1.2×10^4	146
IIb	9.5×10^4	396
IIIb	2.1×10^5	1460

[a]In toluene at 25.0 °C. [b]Equilibrium constants for the binding of 1-MeIm to complexes. [c]Half-saturation pressures for dioxygen binding. [d]Not determined.

of the 1-MeIm plane, the latter is not. When the dihedral angle (ϕ in Fig. 2) is equal to 0°, π-electron donation of the 1-MeIm is expected to be at the maximum because of the maximum π-overlap with Co dπ orbitals [9]. As Walker has reported, the rotation of 1-MeIm in [Fe(α^2-*trans*-TPivPP)(1-MeIm)$_2$]Cl is restricted by pival groups, and the dihedral angle of the bound 1-MeIm is, on the average, equal to 45° [10]. As the 1-MeIm binding site in **IIIb** is identical to that of [Fe(α^2-*trans*-TPivPP)]$^+$, the dihedral angle of the bound 1-MeIm to complex **IIIb** might be 45°. So, the lobe of Co dπ (d_{xz} or d_{yz}) orbitals point to pyrrole nitrogen and the lobe of pπ (p_x or p_y) orbitals on the nitrogen of 1-MeIm point

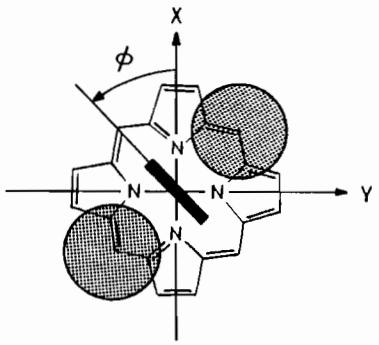

Fig. 2. Schematic representation of the dihedral angle (ϕ) and the coordinate axis system in the 1-MeIm adduct of complex **IIIb**. Cross-dotted circle indicates pival groups and a solid rectangle indicates the 1-MeIm plane.

to $\phi = 135°$. Therefore, the decreased dioxygen affinity of **IIIb** is attributed to the regulated orientation of the 1-MeIm plane ($\phi = 45°$), in which $\pi-\pi$ interaction between Co and 1-MeIm reaches a minimum, due to the steric repulsions with appended pival groups. Such restraint on the orientation of the 1-MeIm plane might be decreased by decreasing the bulkiness of the appended substituents. Consistently, the dioxygen affinities decrease in the order of the bulk of the appended substituents

Details of our work will be published elsewhere.

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