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Syntheses and Characterization of Cobalt(II) Complexes of Dimeric 'Picket Fence' Porphyrins

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Abstract

A series of dimeric picket fence porphyrinatocobalt(II) complexeses in which the length of the bridging chain controls the dioxygen affinity was newly derived from the coupling of two *meso*-mono-(*β-o*-aminophenyl)-tris-(α,α,α-*o*-pivaloylamidophenyl)-porphyrins with $(CH_2)_n(COCl)_2$ (n = 1, 3, 5 or 7). Some of the dimeric complexes form a unique 'sandwich structure' upon binding with certain bidentate ligands, and their dioxygen affinities are greatly increased compared with those for corresponding monomeric complexes. The relationship observed between the length of the bridging chain and the dioxygen affinity of the dimer complex having a sandwich structure is interpreted in terms of the displacement mechanism of the metal atom from a porphyrin plane.

Introduction

Many model compounds have been synthesized and characterized in order to mimic the reversible dioxygen binding to myoglobin (Mb) [1–8]. While myoglobin is monomeric in molecular structure and exhibits a hyperbolic curve upon oxygenation, hemoglobin (Hb) is regarded as a tetramer and reacts with dioxygen cooperatively. In discussing the mechanism of the cooperative effects, the shift of central metal atom to the porphyrin plane by oxygenation has been considered to be one of the important factors in Hb and CoHb [9–13]. In simply confining the correlation to the mechanism, Perutz suggested that the proximal histidine (F8) pulls the iron atom away from the porphyrin plane in the deoxyhemoglobin and thereby reduces its dioxygen affinity (T-state) [13]. He assumed further that the binding of dioxygen to the first site in the deoxyhemoglobin pushes the iron atom up to the porphyrin plane, and subsequent changes to quaternary structure are spread: thus the dioxygen affinities of the remaining sites are functionally increased (R-state).

To explain the Hb model systems, knowledge of a complex which has more than two active sites in a molecule will be needed. Here, the syntheses of a series of dimeric porphyrinato cobalt(II) complexes, each having two identical active centers with a monobridging chain in the molecule, and their dioxygen binding behaviors in the presence of monodentate or bidentate ligand are reported.

Experimental

meso-Mono(*β-o*-aminophenyl)tris(α,α,α-*o*-pivaloylamidophenyl)-porphyrin, H_2-β$am\alpha^3$ pivPP, was prepared according to the literature [14]. *meso*-Tetrakis-(α,α,α,α-*o*-pivaloylamidophenyl)porphyrinatocobalt-(II), [Co(α^4-TpivPP)], and *meso*-tetrakis(α,α,α,*β-o*-pivaloylamidophenyl)porphyrinatocobalt(II), [Co(α^3-TpivPP)], were prepared by the procedure described earlier [15, 8].

Preparation of 5α,10α,15α-tris(o-pivaloylamidophenyl)-20β-(o-valerylamidophenyl)porphyrin, H_2-α^3pivβ-valPP

A solution of H_2-β$am\alpha^3$pivPP (200 mg) in CH_2Cl_2 (30 cm^3) was added to a mixture of pyridine (0.2 cm^3) and valeryl chloride (0.1 cm^3). After 3 h of stirring, 10% NH_4OH (25 cm^3) was added to it, and the solution was stirred for an hour. The organic portion was washed three times with water and then dried with anhydrous sodium sulfate and evaporated to dryness. The resultant solid was dissolved in $CHCl_3$ and chromatographed on a silica-gel column using $CHCl_3$–ether (8:1 volume ratio) as an eluent. The second band was collected and the product was recrystallized from benzene–hexane.

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Preparation of Picket Fence Dimers: bis[(5α,10α,15α-tris(o-pivaloylamidophenyl)-20β-mono(o-phenyl)porphyrin)] methanedicarbamoyl, (PFD-1), 1,3-bis[(5α,10α,15α-tris(o-pivaloylamidophenyl)-20β-mono(o-phenyl)porphyrin)] propanedicarbamoyl, (PFD-3), 1,5-bis[(5α,10α,15α-tris(o-pivaloylamidophenyl)-20β-mono(o-phenyl)porphyrin)] pentanedicarbamoyl, (PFD-5), and 1,7-bis[(5α,10α,15α-tris(o-pivaloylamidophenyl)-20β-mono(o-phenyl)porphyrin)] heptanedicarbamoyl, (PFD-7)

To a solution of H_2-βamα^{3}pivPP (0.27 mmol) in CH_2Cl_2 (40 cm^3), a mixture of pyridine (0.2 cm^3) and $(CH_2)_n(COCl)_2$ (n = 1, 3, 5, or 7) (0.3 mmol) was added. After 3 h of stirring, 10% NH_4OH (25 cm^3) was added to the solution and it was stirred for an hour. The organic layer was washed three times with water, then dried with anhydrous sodium sulfate and evaporated to dryness. The resultant solid was dissolved in benzene, and was chromatographed on a silica-gel column (3 × 25 cm) using benzene–ether (7:1 volume ratio) as an eluent. The second band was collected, and the solvent was removed off by a rotary evaporator. Finally the product was recrystallized from benzene–hexane.

Cobalt Insertion

Dimeric porphyrin or porphyrin (0.1 mmol) was treated with anhydrous $CoCl_2$ (0.3 mmol) in THF (100 cm^3) and 2,6-dimethylpyridine (0.3 cm^3) at 50 °C for an hour under N_2 atmosphere. Purification was carried out by alumina-column chromatography. The results of elemental analyses are listed in Table I.

Measurements

Proton NMR spectra were obtained from a JEOL-MH-100 spectrometer. Electronic spectra were recorded with a HITACHI 340 spectrophotometer. Oxygenation equilibria were determined by spectrophotometric O_2 titration. A sample solution containing a dimeric porphyrinatocobalt(II) complex and an axial base was exposed to various partial pressures of O_2 in a cell mounted with a rubber septum equipped with gas inlet and gas outlet tubes. Various partial pressures of O_2 were obtained by a Gas Mixture (Kofloc model GM-3A). Temperatures were maintained to a precision of ±0.1 °C by the use of a constant-temperature circulation pump (Neslab model RTE-8) passing through a variable-temperature cell holder. Base concentrations were chosen to give >99% of the five-coordinate adduct. Axial base equilibria were determined by the published procedure [8].

Synthesis and Characterization

The precursor, H_2-βamα^{3}pivPP, was treated with 1 equivalent of bridging reagents ($(CH_2)_n(COCl)_2$; n = 1, 3, 5 or 7) in CH_2Cl_2 to give corresponding dimeric porphyrins. Structures and abbreviations used are shown in Fig. 1. The yields of dimeric porphyrins were low, in general, when reactions were carried out in dilute solutions. The use of a small amount of

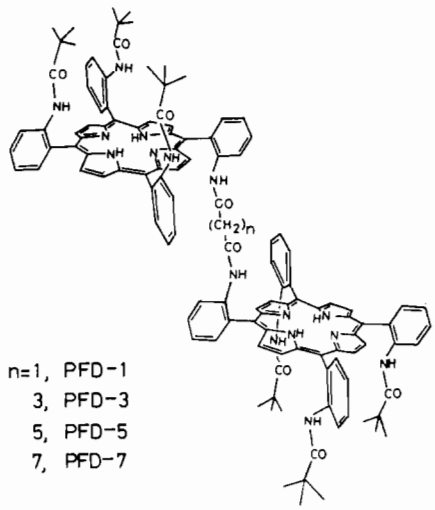


Fig. 1. The dimeric 'picket fence' porphyrins.

TABLE I. Analytical Data

Compound	%C		%H		%N	
	Found	Calc.	Found	Calc.	Found	Calc.
H_2-α^{3}pivβvalPP	75.30	76.01	6.47	6.58	11.00	11.08
PFD-1	75.18	75.60	5.99	6.08	11.60	11.66
PFD-3	74.99	75.75	6.19	6.20	11.18	11.49
PFD-5	75.11	75.89	6.37	6.32	11.14	11.33
PFD-7	76.38	76.02	6.20	6.43	10.52	11.17
[Co(α^{3}pivβvalPP)]	71.38	71.96	5.93	6.04	10.31	10.49
[Co_2(PFD-1)]	70.68	71.38	5.52	5.54	10.41	11.01
[Co_2(PFD-3)]	71.30	71.57	5.61	5.66	10.70	10.86
[Co_2(PFD-5)]	71.09	71.76	5.69	5.78	10.57	10.71
[Co_2(PFD-7)]	71.50	71.94	5.83	5.89	10.29	10.57

TABLE II. ^{1}H NMR Data[a]

	H_2-βamα^{3}pivPP	PFD-1	PFD-3	PFD-5	PFD-7
Methyl protons[b]	0.18	0.12	0.14	0.15	0.16
	0.1	0.06	0.07	0.08	0.08
Pyrrole protons[c]	−2.6	−2.68	−2.74	−2.72	−2.60

[a]Chemical shifts (ppm) from TMS in $CDCl_3$. [b]Methyl protons in pivaloyl groups. [c]Internal pyrrole N–H protons.

TABLE III. Equilibrium Constants for Base Adducts Formation[a]

	[Co(α^3-TpivPP)]	[Co_2(PFD-1)]	[Co_2(PFD-3)]	[Co_2(PFD-5)]	[Co_2(PFD-7)]
PY	1.2×10^3	1.4×10^3	1.2×10^3	1.3×10^3	1.4×10^3
BIPY	9.2×10^2	4.4×10^3	4.4×10^4	4.0×10^4	3.3×10^4
BIPYEt	3.0×10^3	7.1×10^2	3.5×10^4	2.7×10^5	3.3×10^5

[a]In DMF at −15.0 °C. (M^{-1})

CH_2Cl_2 (*ca.* 25 cm^3) was recommended to obtain the dimeric porphyrins in better yield.

^{1}H NMR spectroscopy was a particularly useful technique for establishing the structures of dimeric porphyrins. The chemical shifts of the methyl protons of dimeric porphyrins were virtually identical with that of the precursor, as shown in Table II. So it was confirmed that the geometry of the picket fence was retained upon dimerization. On the conformation with two porphyrin planes, two cannonical structures would be possible (structure **I**, **II**).

I **II**

If the dimeric porphyrins have the structure **I** (face-to-face), the internal pyrrole protons would be shifted upfield, because of the ring current interaction of the two porphyrin rings [16]. In the dimeric porphyrins prepared, no upfield shifts were observed compared with those of the precursor, as shown in Table II. Therefore, it is concluded that these dimeric porphyrins have the structure **II**.

The lack of isomerization during cobalt(II) insertion was checked by ^{1}H NMR measurements on porphyrins in which cobalt(II) ions were removed from complexes by treating with concentrated H_2SO_4. The prepared cobalt(II) complexes of dimeric porphyrins were stable to autoxidation in toluene benzene or even in DMF at room temperature.

Ligand Equilibria and Oxygenation

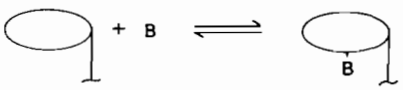
(A) Monodentate ligands

The reactions between dimeric porphyrinatocobalt(II) complexes and monodentate axial bases in solution are as follows:

$$[Co{-}(P{-}P){-}Co] + L \rightleftharpoons [Co{-}(P{-}P){-}Co{-}L]$$

$$[Co{-}(P{-}P){-}Co{-}L] + L \rightleftharpoons [L{-}Co{-}(P{-}P){-}Co{-}L]$$

where (P–P) represents dimeric porphyrins and L the monodentate ligand, respectively. Upon the addition of pyridine into the solution of dimeric porphyrinatocobalt(II) complexes, clear isosbestic points were observed, and the distinction between [Co–(P–P)–Co–L] and [L–Co–(P–P)–Co–L] could not be observed. The equilibrium constants for pyridine (B) binding to the dimeric complexes are calculated according to the following equation:



The experimental results (Table III) show that the variations in length of bridging chains in the dimeric complexes result in little difference in their equilibrium constants for the binding with pyridine as an axial ligand. On the other hand, the dioxygen affinities of dimeric complexes (Table IV) are reduced compared to that of the monomeric complex, [Co(α^3-TpivPP)]. Compared with the dioxygen affinity of [Co(α^3-TpivPP)], a reduction in dioxygen affinity was also observed for [Co(α^3-pvβvalPP)], which has the same methylene chains

TABLE IV. Half-saturation Pressures of Dioxygen Binding[a]

	PY	BIPY	BIPYEt
[Co(α^3-TpivPP)]	600	830	460
[Co(α^3pivβvalPP)]	850	910	630
[Co_2(PFD-1)]	1000	520	680
[Co_2(PFD-3)]	1600	280	290
[Co_2(PFD-5)]	980	400	230
[Co_2(PFD-7)]	1200	460	270

[a]In DMF at −15.0 °C (torr).

as bridging groups in dimeric complexes on the binding site of pyridine. Therefore, no appreciable difference in their equilibrium constants for the binding with these complexes to pyridine was observed. Some reductions observed for their dioxygen affinities could be attributed to a steric environment of the bridging reagent on the binding sites of pyridines.

(B) Bidentate ligands

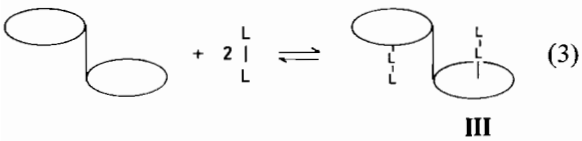
Table III shows the equilibrium constants for axial base adduct formations. In the case of [Co(α^3-TpivPP)], CoP, the following two binding modes are possible for the binding with bidentate ligand, L–L:

$$CoP + L\text{–}L \rightleftharpoons L\text{–}L\text{–}CoP \quad (1)$$

$$2CoP + L\text{–}L \rightleftharpoons PCo\text{–}L\text{–}L\text{–}CoP \quad (2)$$

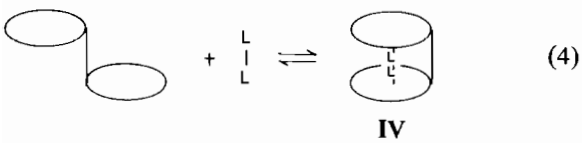
The equilibrium constant for 4,4′-bipyridine (BIPY) or 1,2-bis(4-pyridyl)ethane(BIPYEt) to [Co(α^3-TpivPP)] is comparable to that for pyridine in DMF. A blue shift of the Soret band was not observed upon addition of bidentate ligands to [Co(α^3-TpivPP)]. Therefore, the binding mode of BIPY or BIPYEt to [Co(α^3-TpivPP)] can be represented by eqn. (1).

In the case of the dimeric complexes, two alternative modes would also be possible for the binding of bidentate ligands.



(3)

III



(4)

IV

The equilibrium data in Table IV were calculated with the assumption that the binding modes of the dimeric complexes to bidentate ligands would be represented by eqn. (4).

The equilibrium constants for the bindings with BIPY to dimeric complexes (except for [Co_2(PFD-1)]) have unusually large values compared to the value of [Co(α^3-TpivPP)]. These large values could also be explained as a chelating effect [17] on forming species **IV** (sandwich structure) in eqn. (4). Furthermore, a blue shift (~2 nm) of the Soret band was observed when BIPY was added to the solution of dimeric complexes. This phenomenon provides strong support for the 'sandwich-structure' with the dimeric complexes in the solutions [18].

On the other hand, the smaller equilibrium constant value of [Co_2(PFD-1)], compared to those of other dimeric complexes, suggests that a large amount of species **III** must exist in addition to species **IV**, because the bridging chain in [Co_2(PFD-1)] is not long enough to form species **IV**.

On the binding of BIPYEt to dimeric complexes, it may be concluded from the equilibrium data that both [Co_2(PFD-5)] and [Co(PFD-7)] bind BIPYEt to form species **IV**, while [Co_2(PFD-3)] binds BIPYEt to form both species **IV** and **III** (minor amount), and [Co_2(PFD-1)] binds BIPYEt to form species **III**, respectively.

The dioxygen affinities for BIPY and for BIPYEt adducts of cobalt(II) complexes are listed in Table IV. In the case of using BIPY as an axial ligand, it is noticeable that the dioxygen affinities take a maximum value at [Co_2(PFD-3)], and the value is also comparable to the value of [Co(α^4-TpivPP)]. As in the case of using pyridine as an axial ligand, the dioxygen affinities are reduced compared with those of [Co(α^3-TpivPP)] in both the BIPY and BIPYEt adducts. Among dimeric complexes having sandwich structures in their base adducts, their dioxygen affinities were reduced in the order: [Co_2(PFD-3)], [Co_2(PFD-5)], [Co_2(PFD-7)]. Similarly, in the case of using BIPYEt as an axial ligand the dioxygen affinities are at a maximum for [Co_2(PFD-5)], and their dioxygen affinities are reduced in the order: [Co_2(PFD-5)], [Co_2(PFD-7)].

In order to elucidate the origin of the order of the dioxygen affinities, we discuss the following factors which may account for the regulation of the dioxygen affinities of the model complexes. Among these are: (i) the effect of solvent [5]; (ii) the influence of cavity size [8]; (iii) the electronic effects due to changes in the substituents on the porphyrin rings or axial ligands [19]; (iv) the steric interaction between the axial ligand and the metal ion, hindering the motion of the central metal toward porphyrin plane [2].

From these, (i) and (ii) should be ruled out in this case, because the cavities on the dimeric complexes are of similar size and the same solvent was employed throughout this work. Furthermore, changing the length of the bridging chain would bring about little electronic effect on the porphyrin ring, and since

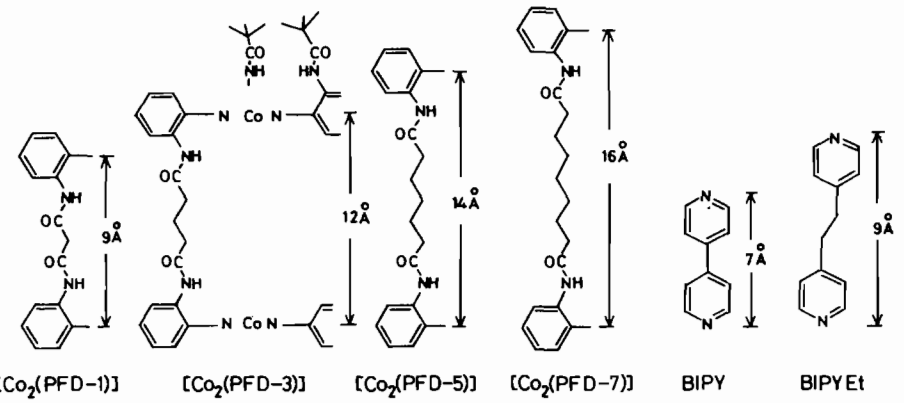


Fig. 2. Schematic representations of dimeric porphyrinatocobalt(II) complexes and bases.

the same base was used in each experiment, the electronic effects which occurred through the series of this work might be equivalent as a result. Therefore, the differences in the dioxygen affinities among the model complexes can be mainly accounted for by the remaining factor, *i.e.*, (iv). Figure 2 shows the molecular sizes of the dimeric complexes and bases.

Assuming the bond length of Co–N (pyridine) is about 2.4 Å [20], it may also be speculated that, for the dimeric complexes having sandwich structures, the displacement of the central cobalt(II) ion from the porphyrin plane in a series of $[Co_2(PFD\text{-}n)]$ (n = 3,5,7) increases in the order $[Co_2(PFD\text{-}3)] < [Co_2(PFD\ 5)] < [Co_2(PFD\text{-}7)]$ in the case of BIPY adducts. In the case of BIPYEt adducts, the order $[Co_2(PED\text{-}5)] < [Co_2(PFD\text{-}7)]$ is expected.

On each bidentate ligand adduct, the orders expected are identical with those of the observed orders of reduction of the dioxygen affinities. This may be attributed to the fact that the skeletal structures between the two bridged porphyrin planes are not so flexible. Therefore, it can be concluded that the increment of the displacement of the central cobalt(II) ion from the porphyrin plane reduces the dioxygen affinities of the dimeric complexes.

Although a difference between the dioxygen affinities of the first and second dioxygen binding sites on the dimeric complexes having sandwich structures might be also expected, no appreciable difference was observed in this series of experiments. Perhaps these kinds of differences might be too small to detect. A similar approach along this line will be necessary with more suitable new model complexes.

Finally, we also add note that the dioxygen affinities of dimeric complexes having a sandwich structure are higher than those of monomeric complexes. This finding may suggest that there are some unfavorable intramolecular strains even in base adducts of $[Co(\alpha^3\text{-TpivPP})]$ or $[Co(\alpha^3 piv\beta valPP)]$ with bidentate ligands. As mentioned above, we inferred that the displacement of a metal atom from a porphyrin plane would be mainly responsible for this kind of unfavorable intramolecular strain. However, some of the remaining unfavorable strains might be released in the case of dimeric complexes having a sandwich structure. Binding of dioxygen at the first site will decrease this strain somewhat, and the dioxygen affinity of the remaining site in the dimeric model complexes will be effectively increased.

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