O_2 and CO Binding to a New Type of Iron(II) Porphyrins

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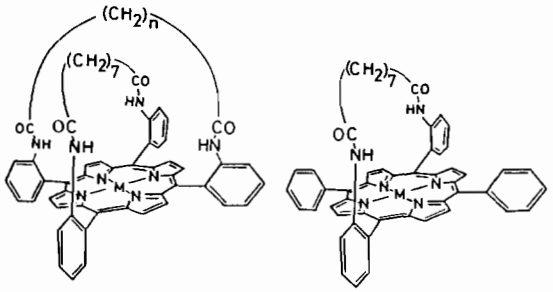
In hemoproteins, the discrimination against the binding of CO relative to that of O_2 plays an important role in preventing poisoning by CO. Distal effects [1] functionally produced by globin are thought to be a major motive force for this discrimination and can be separated into two effects: polar and steric. To elucidate the role of these effects on the discrimination, studies [2–5] have been carried out using wide varieties of model porphyrins on the effects upon the discrimination. Nevertheless, whether so-called 'cavity' within globin discriminates between O_2 and CO by a steric effect is still unresolved [2a, 4b]. To clarify further the steric effect, a series of model porphyrins were designed and synthesized with the unique structure in which one aliphatic chain crosses over another aliphatic chain bridging the same side of a porphyrin plane (Fig. 1).



IIa $n = 14$, M = 2H **IVa** M = 2H
IIb $n = 14$, M = Fe **IVb** M = Fe
IIIa $n = 18$, M = 2H
IIIb $n = 18$, M = Fe

Fig. 1. Model porphyrins.

The discrimination between O_2/CO binding by steric effect was studied experimentally on these model porphyrins.

5α,15α-Bis(2-aminophenyl)-10α,20α-(2,2′-nonanediamidodiphenyl)porphyrin, (**I**) was prepared from the isomerization of 2-aminophenyl groups of its 5β,15β-isomer [6]. Porphyrins **IIa** and **IIIa** were synthesized from coupling **I** with $(CH_2)_n(COCl)_2$ ($n = 14$ or 18) under high dilution conditions [6, 7]. Porphyrin **IVa** was prepared by the reported method [8]. All new compounds described gave spectral (FAB mass, ^{1}H NMR) and analytical data in accordance with their assigned structures. It is expected that the $-(CH_2)_{14}-$ or $-(CH_2)_{18}-$ chain in **IIa** or **IIIa** gives steric repulsion to the heptane chain and makes the chain close to the porphyrin ring. Also the heptane chain of **IIa** is expected to receive more severe steric repulsion than that of **IIIa**, because the crossing over chain of **IIa** (*i.e.* the $-(CH_2)_{14}-$ chain) is shorter than the $-(CH_2)_{18}-$ chain of **IIIa**. This expectation was confirmed by ^{1}H NMR measurements. As shown in Table I, the methylene proton signals at the 4-position in the heptane chain of **IIa** and **IIIa** shift upfield by 1.24 and 0.62 ppm, respectively, compared to that of **IVa**. These upfield shifts are the result of the ring current of porphyrin [9], so the heptane chain of **IIa** is suggested to be more crushed than that of **IIIa**. Iron insertions into **IIa** or **IIIa** and **IVa** were accomplished by heating **IIa** or **IIIa** in acetic acid and **IVa** in tetrahydrofuran, respectively, with $FeBr_2$. Purifications of iron(III) porphyrins were carried out by silica-gel column chromatography. Fe(III) complexes were reduced to Fe(II) complexes by aqueous sodium dithionite in a two-phase system [3a] (toluene–water) under Ar in the presence of 1,2-dimethylimidazole (1,2-Me_2Im). The Fe(II) complexes prepared in this study bind O_2 or CO reversibly in toluene at 20 °C in the presence of 1,2-Me_2Im and their half-saturation pressures for O_2 or CO binding were obtained by spectroscopic titrations [6] (Fig. 2 and Table II).

The O_2 affinity of **IIIb** is slightly higher but the CO affinity is 2-fold lower than that of **IVb**. Also the O_2 and CO affinities of **IIb** are about 100 and 600 times lower, respectively, than those of **IIIb**. That is, **IIb** reduces CO affinity selectively and has a remarkably low value of $M = 24$. Recently, Traylor *et al.* [4b] reported the model complex 3,5-pyridine-5,5-hemecyclophane, which has a small M value. They proposed that a polar effect induced by pyridine is the principal factor in the discrimination. The changes in O_2 and CO affinities between **IIIb** and **IVb** can be explained by the difference in local polarity. That is, the cavity of **IIIb** must be more

TABLE I. ^{1}H NMR Data[a] for Nonanediamido Groups in Porphyrins

Porphyrins	Methylene protons[b]				Amido protons
	1,7-	2,6-	3,5-	4-	
IVa	1.16	−0.51	−1.24	−2.51	5.99
IIIa	1.25	−1.16	−1.51	−3.13	6.31
IIa	1.21	−1.58	−1.58	−3.75	6.45

[a]Chemical shift (ppm) from TMS in $CDCl_3$. [b]Numbers refer to positions in the heptane group.

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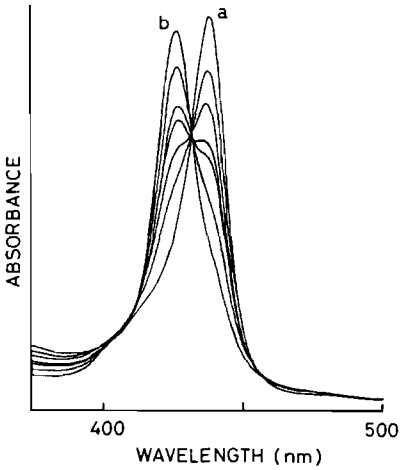

Fig. 2. Determination of $P_{1/2}$ (CO) for **IIb**: 0.5 M 1,2-dimethylimidazole in toluene at 20 °C: (curve a) under 1 atom of N_2; (curve b) CO partial pressure of 395 torr. The following partial pressures of CO were used: 16.0, 31.4, 60.3, 81.2 and 161 torr.

TABLE II. O_2 and CO Binding to Iron(II) Complexes

Complexes[a]	$P_{1/2}$ (O_2)[b] (torr)	$P_{1/2}$ (CO)[b] (torr)	M[c]
IVb	18	0.05	360
IIIb	15	0.09	170
IIb	1400	62	23

[a]Solutions are 0.5 M 1,2-dimethylimidazole in toluene at 20 °C. [b]$P_{1/2}$ (O_2) and $P_{1/2}$ (CO) are half-saturation pressures for O_2 and CO binding, respectively. [c]M = $P_{1/2}$ (O_2)/$P_{1/2}$ (CO).

polar than that of **IVb**, because **IIIb** has two more amido groups in the cavity than **IVb** has. On the contrary, the discrimination reaction observed in **IIb** may be responsible for steric hindrance to bound O_2 and CO, respectively, for the following reasons. The change in the polarity within cavities between **IIb** and **IIIb** is small compared to that between **IIIb** and **IVb**, since both **IIb** and **IIIb** have four similar amido groups. On the other hand, ^{1}H NMR results for free base porphyrins imply that the strapped heptane chain is crushed in the order **IVb** (without crushing) < **IIIb** < **IIb**, and the steric hindrance to bound O_2 and CO will be increased in the same order. In particular, the Fe–CO bond unit prefers to be linear and normal to the porphyrin plane in Fe(II)–porphyrin systems, whereas O_2 binds in a bent fashion [2]. Therefore the Fe–CO unit will receive more severe steric hindrance than that of the Fe–O_2 one. Thus, it is concluded that steric hindrance induced by the crushed heptane chain in **IIb** causes a remarkable reduction in CO affinity but a minor one in O_2 affinity, respectively.

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