Oxygenation of a New Bis-fenced Porphyrinato Iron without Amide Groups: 5,10,15,20-Tetrakis(2,6-bispivaloyloxyphenyl)porphyrinatoiron(II)

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A new porphyrinatoiron complex, 5,10,15,20-tetrakis(2,6-bispivaloyloxyphenyl)porphyrinatoiron(II), has been synthesized; axial–base ligation was sterically depressed by the four ester groups on each side of the porphyrin plane and a stable dioxygen adduct formed reversibly at 25 °C in toluene.

As model compounds for haemoglobin (Hb) and myoglobin (Mb), many synthetic haem compounds have been prepared and their dioxygen- or carbon monoxide-binding discussed.[1—8] The first successful model was the 'picket-fence porphyrin,'[1] in which the pivalamido fences are believed to prevent bimolecular irreversible oxidation and to provide the distal moiety with hydrogen bonding with a bound dioxygen. However, there remain a couple of queries as to whether a haem hindered on both faces would serve as a more stable dioxygen carrier and whether the distal amide residue is

Table 1. Ligation equilibria constants, and oxygen-affinity and thermodynamic parameters for iron(II) and cobalt(II) porphyrin complexes in toluene at 25 °C.

Porphyrin	Ligand	K_B/ mol^{-1} dm^3	$K^B{}_B$/ mol^{-1} dm^3	P_{50}/ mmHg	ΔH/ kcal mol^{-1}	ΔS/ cal K^{-1} mol^{-1}
(**1b**)	1-MeIm	13	50	56	—	—
(**1b**)	1,2-Me_2Im	36	—	866[a]	−9.3	−31
Fe(pp)[b]	Im	8.8×10^3	7.9×10^4	—	—	—
Fe(piv)(pp)[c]	1,2-Me_2Im	3.2×10^4	—	38	−14.3	−42
Fe(bp)(pp)[d]	1,2-Me_2Im	2.7×10^4	—	508	−14.4	−47
Fe(piv)$_2$(C_8)[e]	1-MeIm	1.5×10^5	—	1.0×10^{-1}	—	—
(**1c**)	1-MeIm	5	—	136[f]	—	—
Co(piv)(pp)[g]	1-MeIm	1.7×10^4	—	140	−12.2	−38

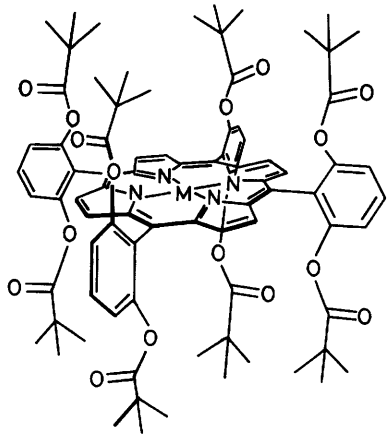
[a] Calculated from thermodynamic values. [b] Fe(pp): 5,10,15,20-tetraphenylporphyrinatoiron(II). From ref. 7. [c] Fe(piv)(pp): 5,10,15,20-tetrakis(pivalamidophenyl)porphyrinatoiron(II). From J. P. Collman, J. I. Brauman, K. M. Doxsee, T. R. Halbert, and K. S. Suslick, *Proc. Natl. Acad. Sci. USA*, 1978, **75**, 564. [d] Fe(bp)(pp): 5,10,15,20-tetrakis(2,4,6-triphenylphenyl)porphyrinatoiron(II). From ref. 5. [e] Fe(piv)$_2$(C_8): α-(octanediamido)diphenyl-α,α-bis(pivalamidophenyl)porphyrinatoiron(II). From ref. 3. [f] In CH_2Cl_2 at −66°C. [g] Co(piv)(pp): 5,10,15,20-tetra(pivalamidophenyl)porphyrinatocobalt(II). From ref. 11.

essential for stable dioxygen-binding.[2,5,7,8] A unique model in which the bulky protective groups were linked through the β-position of the pyrrole units has been synthesized and gave a stable dioxygen adduct only in amide type solvents.[7]

We now report the synthesis of a new tetraphenylporphyrin hindered with ester groups on both faces, 5,10,15,20-tetrakis(2,6-bispivaloyloxyphenyl)porphyrin (**1a**), and its iron (**1b**) and cobalt (**1c**) complexes; the axial–base ligation profile and stable dioxygen adduct formation at 25 °C in toluene are described. The highly symmetrical porphyrin (**1a**) was designed to remove the complexity of diastereoisomeric properties in the preparation of substituted tetraphenylporphyrins. 5,10,15,20-Tetrakis(2,6-dimethoxyphenyl)porphyrin (**2**) was prepared by condensation of pyrrole with 2,6-dimethoxybenzaldehyde in heated propionic acid.[9] Compound (**2**) was demethoxylated by boron tribromide to give 5,10,15,20-tetrakis(2,6-dihydroxyphenyl)porphyrin (**3**). Compound (**3**) was allowed to couple with pivalic anhydride in the presence of 4-dimethylaminopyridine to yield (**1a**).† Treatment of (**3**) with $FeCl_2$ and reaction with pivalic anhydride as in the preparation of (**1a**) gave (**1b**),† and similar treatment of (**3**) with $CoCl_2$ followed by reaction with pivalic anhydride gave (**1c**).† The Fe^{III} porphyrin (**1b**) was dissolved in toluene and reduced by shaking with aqueous $Na_2S_2O_4$ under N_2. The aqueous layer was discarded and the toluene solution dried (Na_2SO_4): $\lambda_{max.}$ (toluene) 565, 535, 440, and 413 nm.

Titration of the four-co-ordinate porphyrinatoiron(II) with 1,2-dimethylimidazole (1,2-Me_2Im) in toluene under N_2 at 25 °C gave the corresponding five-co-ordinate complex ($\lambda_{max.}$ 558, 535, and 436 nm) with well defined isosbestic points (420 and 371 nm). Titration of the four-co-ordinated porphyrinatoiron(II) by 1-methylimidazole (1-MeIm) was complicated by the simultaneous formation of five- and six-co-ordinated complexes; the spectroscopic data were analysed by the mathematical method described by Rougee and Brault.[10]

Equilibrium constants of the imidazole derivative (K_B, $K^B{}_B$) were smaller than those of the unprotected porphyrin (*meso*-tetraphenylporphyrin),[10] one-face protected porphyrin (picket-fence porphyrin)[1,11] and both-faces protected porphyrin (bis-pocket porphyrin)[5] (Table 1). This result shows that 2,6-dipivaloyloxy substituents encumber more effectively both axial sites on the porphyrin plane than do other substituents.



(**1a**) M = 2H
(**1b**) M = Fe
(**1c**) M = Co

The visible absorption spectrum of the deoxy (**1b**)/1-MeIm complex changed to that of the dioxygen adduct on exposure to dioxygen [$\lambda_{max.}$ (toluene) deoxy: 561, 535, and 429 nm; oxy: 544 and 423 nm]. The dioxygen adduct changed to the corresponding CO adduct on bubbling carbon monoxide gas through the solution [$\lambda_{max.}$ (toluene) 542 and 425 nm]. The half-life of the dioxygen adduct with respect to irreversible oxidation at 25 °C was 26 h. The (**1b**)/1,2-Me_2Im and (**1c**)/1-MeIm complexes could form a dioxygen adduct only at low temperature owing to their low oxygen-binding affinity. Both complexes bound and dissociated dioxygen reversibly with increasing or decreasing temperature and during this cycle no irreversible oxidation *via* a bimolecular process was observed. This indicates that the bulky ester groups on both sides of the porphyrin are effective in impeding the formation of an intermediate μ-dioxo-dimer.

The oxygen-binding affinity (P_{50}; dioxygen pressure at half oxygen-binding for the porphyrinatometal) of (**1b**) or (**1c**) was determined by analysing the spectral data by Drago's equa-

† *Spectroscopic data* for (**1a**): δ_H (400 MHz, $CDCl_3$, Me_4Si) −2.8 (2H, s, inner H), −0.3 (72H, s, pivaloyl), 7.4—7.9 (12H, m, phenyl H), and 8.8 (8H, s, pyrrole); *m/z* 1415 (M^+); $\lambda_{max.}$ ($CHCl_3$) 637, 583, 536, 507, and 412 nm. (**1b**): *m/z* 1503 (M^+); $\lambda_{max.}$ ($CDCl_3$) 680, 650, 579, 508, and 416 nm. (**1c**): *m/z* 1472 (M^+); $\lambda_{max.}$ ($CHCl_3$) 554 (sh.), 523, and 404 nm. Satisfactory elemental analyses were obtained for (**1a—c**).

tion.[12] Polar pocket effects or the amide effect have been discussed in relation to the oxygen affinity of the picket-fence porphyrinatoiron complex.[13] The apolar fence in the bis-pocket porphyrinatoiron reduced the oxygen-binding affinity in comparison to the picket-fence complex having polar amide groups in the pocket. The P_{50} values of (**1b**) and (**1c**), having bulky ester groups, were lower than those of other synthetic analogues of Hb. It is assumed that the low oxygen-binding affinity arises because of the nature of the binding site pocket, which had no amide groups, probably leading to hydrogen bonding or dipole–dipole interaction with bound dioxygen.

Table 1 also shows the thermodynamic parameters for the dioxygen binding, which were determined by van't Hoff plots. The enthalpy (ΔH) and entropy changes (ΔS) for the dioxygen binding of the (**1b**)/1,2-Me_2Im complex were estimated to be -9.3 kcal mol^{-1} and -31 cal K^{-1} mol^{-1}, respectively (1 cal = 4.184 J). The values of ΔH and ΔS are both higher for (**1b**)/1,2-Me_2Im than for the other metalloporphyrins. This indicates the formation of a rather weak dioxygen adduct. In comparison with the picket-fence porphyrin, the diminished oxygen-binding affinity of (**1b**) is primarily enthalpic.

Our results show that (**1b**) and (**1c**), which have no amide groups around the bound dioxygen, formed dioxygen adducts which were stable towards irreversible oxidation. The low oxygen-binding affinity is possibly attributed to either the difference in the spacer groups between the porphyrin and the t-butyl radical, *i.e.* amide and ester groups, or reduced imidazole-binding to an iron sterically restrained by the bulky groups around the imidazole-binding site.

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