Synthesis and dioxygenation of [5,10,15,20-tetrakis(α,α,α,α-*o*-pivaloyloxynaphthyl)porphinato]iron(II) with a covalently bound imidazolylalkyl group

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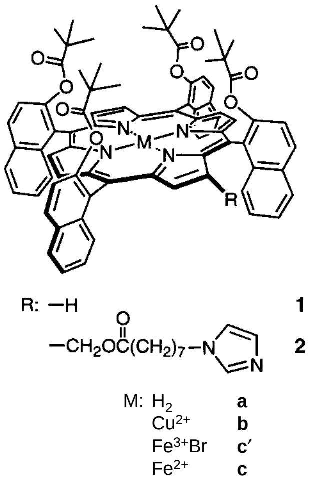
Intramolecular *N*-imidazole coordinated [5,10,15,20-tetrakis(α,α,α,α-*o*-pivaloyloxynaphthyl)porphinato]iron(II) forms a stable dioxygen adduct in toluene at 25 °C; the sterically regulated coordination of the axial base leads to the low electron donation from the central iron to the bound O_2.

Synthetic tetraphenylporphinatoiron (FeTPP) derivatives have been extensively used for the study of hemoprotein analogs, because of their stability and advantage of covalent modification.[1] In particular, the design of both-faces encumbered models has been a topic of great interest for the preparation of stable O_2 carrying hemes.[2–5] The double-sided hindered porphyrins have actually prevented the undesired μ-oxo dimer formation. Symmetric 2,6-disubstituted TPPs are useful precursors, but the total synthetic yields to construct different structures on each side of the porphyrin plane are rather low.[6,7] In order to simply provide a second cavity under the porphyrin macrocycle, we have introduced *o*-substituted α-naphthyl groups to the four *meso*-positions. Non-substituted (tetranaphthylporphinato)iron(II) or (tetraanthracenylporphinato)iron(II) itself, however, cannot form a stable O_2 adduct at ambient temperature.[8,9] Basolo and coworkers only reported the dioxygenation of the single-face capped (naphthylporphinato)iron(II) at 0 °C.[10] Herein, we report for the first time, the synthesis, characterization and reversible O_2 coordination of [tetrakis(*α*,*α*,*α*,*α*-*o*-substituted-naphthyl)porphinato]iron(II) with covalently bound imidazolylalkyl chains at 25 °C.



The precursor porphyrin, tetrakis(β-naphthol)porphine, was prepared by Lindsey's procedure from pyrrole and 2-methoxy-1-naphthaldehyde followed by removal of the methyl groups with BBr_3.[11,12] The *α*,*α*,*α*,*α*-isomer separated by column chromatography was condensed with pivaloyl chloride in THF at 65 °C, giving 5,10,15,20-tetrakis(*α*,*α*,*α*,*α*-*o*-pivaloyloxynaphthyl)porphine **1a** (71%). Introduction of imidazolylalkyl chains to the β-pyrrolic position of the porphyrin was performed according to our previously reported procedure with 8-imidazolyl-1-yl-octanoic acid.[13] For initial formylation, the copper(II) complex **1b** gave a high yield in the Vilsmeir reaction (97%). The obtained 2-formyl–**1b** was, however, rapidly decomposed in H_2SO_4/CH_2Cl_2, which is a typical copper removal condition. All attempts for demetallation of the 2-formyl-**1b** failed. These are in sharp contrast to the 2-formyl–[tetrakis(pivalamidophenyl)porphinato]copper(II) result.[13] Fortunately, we found that the direct Vilsmeir reaction with free base **1a** yielded 2-formyl–**1a** in 21% yield. Iron insertion was carried out using $FeBr_2$ in dry THF affording **2c′**, which is now available in gram quantities. The analytical data of all compounds described above were satisfactory obtained.

2c′ was converted to the iron(II) complex **2c** by reduction in a heterogeneous two-phase system (toluene/aqueous $Na_2S_2O_4$) under an N_2 atmosphere.[7] The UV–VIS absorption spectrum of the orange solution showed five-N-coordinated iron(II) species (λ_{max} = 439, 541, 562 nm, Fig. 1), which was constant in the range of 10 μmol dm^{-3}–3 mmol dm^{-3} at 10–70 °C. The paramagnetic $S = 2$ state of **2c** was evidenced by the β-pyrrolic proton signals at δ 46.8–59.4 downfield to TMS (25 °C).[14] No peaks were seen between δ -5 and -15, showing that a square planar iron(II) porphyrin ($S = 1$) did not exist. Consequently, we can conclude that **2c** is a five-coordinated complex *via* intramolecular imidazole binding under an N_2 atmosphere.

When O_2 or CO binds to **2c**, the resulting complexes are diamagnetic and the ^1H NMR spectra represented characteristics of $S = 0$. Its UV–VIS absorption also changed to those of the O_2 or CO adduct immediately upon exposure to O_2 or CO (Fig. 1). The dioxygenation was kinetically sufficiently stable and reversible at 25 °C depending on the O_2 partial pressure. Oxidation to iron(III) porphyrin, however, took place slowly (half-life ≈ 22 h at 25 °C). The final product was the $Fe^{III}(OH)$

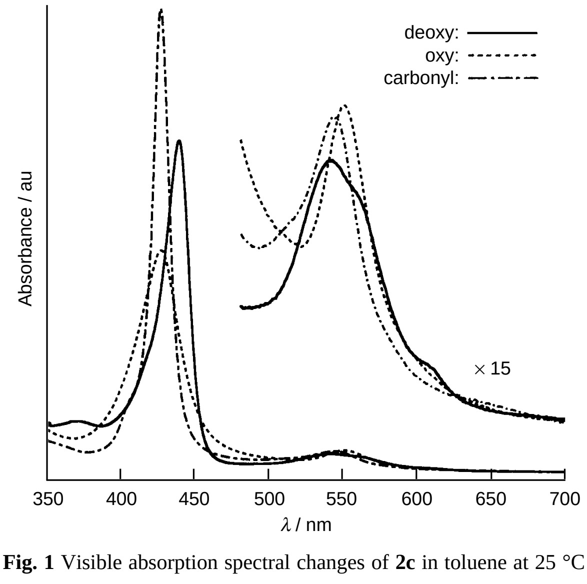


Fig. 1 Visible absorption spectral changes of **2c** in toluene at 25 °C

Table 1 O_2 and CO binding parameters for **2c** in toluene at 25 °C

	O_2			CO	
	$P_{1/2}$/ Torr	$10^{-7}k_{on}$/ $dm^3\ mol^{-1}\ s^{-1}$	$10^{-3}k_{off}$/ s^{-1}	$10^4P_{1/2}$/ Torr	$10^{-6}k_{on}$/ $dm^3\ mol^{-1}\ s^{-1}$
2c	18	2.4	5.0	1.5	3.3
Fe^{II}(TpivPPIm)[a]	0.29	64	1.4	—	31

[a] Ref. 13.

complex with λ_{max} at 420 and 567 nm.[15] The α-naphthalene rings obviously prevent μ-oxo porphyrin dimer formation. The rates of oxidation are strongly sensitive to water content, which is present in organic solvents when the two-phase preparation is used. From the results of the molecular simulation, the total energy of the **2c** μ-oxo-dimer was also extremely high and unlikely to be produced.

The O_2 and CO binding affinities [$P_{1/2}(O_2)$, $P_{1/2}(CO)$] were determined based on the UV–VIS absorption spectral changes (Table 1). The $P_{1/2}(O_2)$ value was 18 Torr at 25 °C, which is 60 times larger than that of [2-imidazolyloctanoyloxymethyl-5,10,15,20-tetrakis(α,α,α,α-*o*-pivalamidophenyl)porphinato]-iron(II) [Fe^{II}(TpivPPIm), $P_{1/2}(O_2)$ = 0.29 Torr].[13] The thermodynamic parameters of the dioxygenation of **2c** were also measured; $\Delta H° = -68$ kJ mol^{-1} and $\Delta S° = -136$ J K^{-1} mol^{-1}. Laser flash photolysis gave the association and dissociation rate constants (k_{on}, k_{off}) of these gaseous molecules.[13,16c,17] We considered that the low O_2 and CO binding affinities are mainly caused by two reasons, (*i*) the sterically regulated imidazole coordination by α-naphthyl groups and (*ii*) the relatively crowded pivaloyloxy cavity around the O_2 binding site. The following results clearly support these assumptions. (*i*) The equilibrium constant for 1,2-dimethylimidazole binding to **1c** (3×10^3 dm^3 mol^{-1}) was sterically hindered and one order of magnitude lower than those of the non-substituted Fe^{II}(TPP) or Fe^{II}(TpivPP).[10,16a] (*ii*) In the IR spectra, the coordinated CO or O_2 to **2c** showed a ν_{CO} at 1976 cm^{-1} ($\Delta\nu_{1/2}$ = 12 cm^{-1}) and a $\nu_{^{16}O_2}$ at 1169 cm^{-1} ($\Delta\nu_{1/2}$ = 11 cm^{-1}); the shifts in the stretching frequencies of $^{16}O_2$ and $^{18}O_2$ adducts (70 cm^{-1}) were in good agreement with Hooke's law. These values are significantly higher than other model hemes.[16b] The differences are probably due to the low π-back donation from the central iron, indicating weak coordination of the *trans* imidazole in **2c**. (*iii*) Kinetically, the low $k_{on}(O_2)$ leads to the low binding affinities of O_2. Based on the earlier important studies,[16c,17] the distal steric hindrance only reduces the association constant for O_2. The pivaloyloxy groups of **2c** are therefore more tilted in comparison to the pivalamide residues of Fe^{II}(TpivPPIm).

The structure of the dioxygenated **2c** complex was then simulated.[18] The dihedral angles of the four α-naphthyl groups with respect to the porphyrin plane are 75–83°, indicating the presence of an apolar space with a depth of *ca.* 4.5 Å under the porphyrin macrocycle. The imidazole coordination to the central iron is definitely oriented to avoid the four bulky naphthalene walls. It is also remarkable that the imidazole plane is unusually tilted from the Fe–N(Im) vector (*ψ*) with an angle of *ca.* 150°, which can not be seen in the same calculation of any other dioxygenated Fe^{II}(TPP) compounds [*e.g.* Fe^{II}(TpivPPIm)]. We considered that the unique tilting geometry of the imidazole ring may be related to the low electron donation from the central iron to the bound O_2 or CO.

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Notes and References

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