Novel Ligand Orientations in Pyridine and Imidazole Complexes of a Highly Substituted Nonplanar Porphyrin, and Implications for the Design of Porphyrins as Regio- and Stereo-specific Oxidation Catalysts

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Specific orientations are observed for pyridine and imidazole ligands complexed to a highly substituted nonplanar porphyrin, suggesting that suitably designed nonplanar porphyrins might be used to direct substrates and increase regio- and stereo-specificity in porphyrin catalysed oxidation reactions.

There is currently speculation that nonplanar conformational distortions of porphyrins and related tetrapyrroles may have an important functional role in biological systems.[1] It has also been suggested that the orientation of axial histidine ligands might be important for modulating the spectroscopic and possibly the redox properties of haem proteins.[2,3] Recent investigations of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetraphenylporphyrin (OETPP; Fig. 1), which adopts extremely nonplanar conformations both in the crystalline state and in solution,[4–8] have shown that this porphyrin is a useful model for probing the effects of nonplanar conformational distortions. Here we report that the axial ligands complexed to OETPP adopt novel orientations, and show that in some cases hindered ligand rotation can be observed. This behaviour is unusual because hindered ligand rotation is normally seen only for complexes with bulky porphyrin substituents or sterically hindered ligands such as 2-methylimidazole.[2,3]

The series of complexes investigated is shown in Fig. 1. Cobalt(III) complexes were chosen for study because they are diamagnetic, and have ligand exchange which is slow on the NMR timescale. Proton NMR assignments for the complexes are given in Table 1. Note that upon cooling the porphyrin methylene protons become diastereotopic as inversion of the macrocycle is slow on the NMR timescale[4] ($\Delta G^*_{\text{Porphyrin Inversion}}$ = 51.5–56.1 kJ mol^{-1}). Significantly, additional porphyrin signals are then seen for the 3Ph-Py and 3Cl-Py complexes, indicating hindered ligand rotation (Table 1).

Attempts to obtain crystal structures of the pyridine or imidazole complexes were unsuccessful. Molecular mechanics calculations were therefore used to investigate the orientations of the axial ligands. The force-field employed in the calculations is known to accurately reproduce the crystal and solution structures of metal complexes of OETPP[4,6–8] and other highly substituted porphyrins.[9] The energy minimized structure obtained for the pyridine complex of Co^{III}(OETPP) is shown in Fig. 2. The saddle conformation of the macrocycle is similar to that seen in the crystal structures of metal complexes of OETPP.[4,6,7] Unusually, the pyridine ligands are oriented approximately parallel to cavities formed by the nonplanar porphyrin macrocycle. Complexes with 3Ph-Py, 3Cl-Py, 1Me-Im and 4Ph-Im ligands gave similar minimum energy structures.

By constraining the ligands to be out of the cavity, the barriers for ligand rotation ($\Delta E_{\text{Rotation}}$) were estimated (Table 1). As expected the calculated energies reached a maximum when the ligand was at 90° to the cavity, and steric repulsions between the ligand and porphyrin dominate the rotational barrier. The calculations also showed that the increased barrier for the pyridine versus imidazole ligands arises partly from close contacts between the 2,6-hydrogens of pyridine and the atoms of the porphyrin core (particularly the nitrogen atoms). The lower rotational barriers calculated for the imidazole ligands suggest that additional porphyrin signals are not observed because ligand rotation is fast on the NMR timescale. Furthermore, the lower rotational barrier calculated for 3Cl-Py *vs.* Py indicates that it is the asymmetry of the ligand rather than the steric influence of the 3-substituent that allows hindered rotation to be observed.

Proton NMR studies were consistent with the structures obtained from the molecular mechanics calculations. The number of additional porphyrin signals seen for the 3Ph-Py and 3Cl-Py complexes agrees with the number expected for a structure in which the ligands are oriented parallel to the porphyrin cavities. Furthermore, upon changing to non-aromatic ligands (*e.g.* 4-methylpiperidine) a significant downfield shift is seen for the porphyrin methyl protons, whereas the other porphyrin protons show much smaller chemical shift changes. This is consistent with the porphyrin methyl protons experiencing an upfield ring current shift from the axial

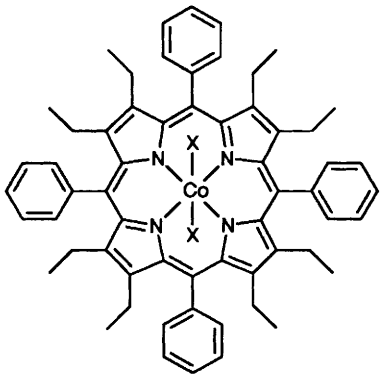

Fig. 1 Structures of amine complexes of Co^{III}(OETPP): X = pyridine (Py), 3-phenylpyridine (3Ph-Py), 3-chloropyridine (3Cl-Py), 1-methylimidazole (1Me-Im), and 4-phenylimidazole (4Ph-Im)

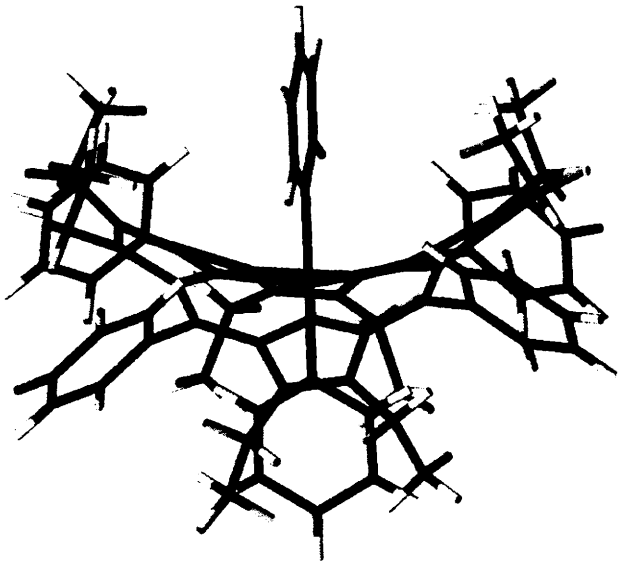

Fig. 2 Calculated minimum energy structure for the pyridine complex of Co^{III}(OETPP)

Table 1 Proton chemical shifts, macrocyclic inversion barriers, and calculated energies for amine complexes of CO^{III}(OETPP).[a]

	Proton	Py	3Ph-Py	3Cl-Py	1Me-Im	4Ph-Im
Porphyrin	H_o	8.16	8.10 (4)[b]	8.17 (4)[b]	8.21	8.12
	H_m	7.71	7.67	7.70	7.70	7.57
	H_p	7.76	7.74	7.70	7.76	7.65
	CH_2	2.23	2.20 (m)[b]	2.29	2.18	2.11
	Me	−0.05	−0.15 (4)[b]	0.00	0.01	−0.07
Ligand	H1	—[c]	—[c]	—[c]	2.18	—[c]
	H2	2.56	2.74	2.61	2.44	2.51[d]
	H3	5.26	—	—	—[c]	11.16
	H4	6.21	6.42	6.28	1.99	—
	H5	5.26	5.35	5.28	4.76	2.02[d]
	H6	2.56	2.53	2.54	—	—
	$\Delta G^*_{\text{Porphyrin Inversion}}$	51.5	52.7	54.8	56.1	55.2
	$E_{\text{Minimum}(°)}$[e]	11.0	12.1	13.9	1.6	3.2
	$E_{0.0°}$[f]	0.0	0.0	0.9	0.7	0.0
	$E_{22.5°}$	2.1	2.1	1.3	2.8	2.8
	$E_{45.0°}$	25.5	29.3	21.8	18.1	18.3
	$E_{67.5°}$	70.3	79.1	64.4	42.6	44.6
	$E_{90.0°}$ ($\Delta E_{\text{Rotation}}$)	107.4	128.5	101.7	60.2	65.0

[a] Proton NMR spectra (δ 300 MHz, CD_2Cl_2, 298 K). The $CHDCl_2$ signal (δ 5.30) was used as an internal reference. The chemical shifts were essentially independent of the anion in the complex, which was typically chloride or iodide. Energies are given in kJ mol^{-1}. [b] Figures in parentheses indicate the number of signals when porphyrin inversion is slow on the NMR timescale (m = multiple overlapping signals). The greater number of signals resolved for the 3Ph-Py complex probably reflects the anisotropic nature of the phenyl substituent. Additional signals were not observed for the Py, 1Me-Im, and 4Ph-Im ligands at temperatures down to 193 K. [c] Position of complexing ligand nitrogen atom. [d] Assignments may be interchanged. [e] Mean angle between the porphyrin cavity and the plane of the axial ligand in the global minimum energy structure. At 0.0° the ligand is parallel to the cavity, at 90.0° the ligand is perpendicular to the cavity. [f] Minimum energy structure when one ligand is constrained at the angle shown. Energy is relative to the global minimum energy structure.

ligands because the ligands are oriented parallel to the porphyrin cavities. The average upfield shift observed for the porphyrin methyl protons (0.46 ppm) agrees well with a shift of 0.33 ppm calculated using a dipole model of the ring current in benzene[10] to represent the ligand ring currents.

From the molecular mechanics calculations and NMR studies reported here, it is clear that the cavity structure of the OETPP macrocycle plays an important role in determining the orientations of the axial pyridine and imidazole ligands. It is interesting to speculate whether porphyrins with cavity structures might also bind substrates selectively on the basis of their shape or size. In theory, this approach could provide improved regiospecificity in porphyrin catalysed oxidation reactions.[11] Non-planar porphyrins might also be prepared with cavities lined by chiral groups, potentially allowing oxidation reactions to be carried out with a high degree of stereospecificity.[12] To investigate these possibilities, several highly substituted nonplanar iron(III) porphyrins are being synthesised, and evaluated as regio- and stereo-specific oxidation catalysts.

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