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A Pyridine-Sensitive Venus Flytrap Porphyrin

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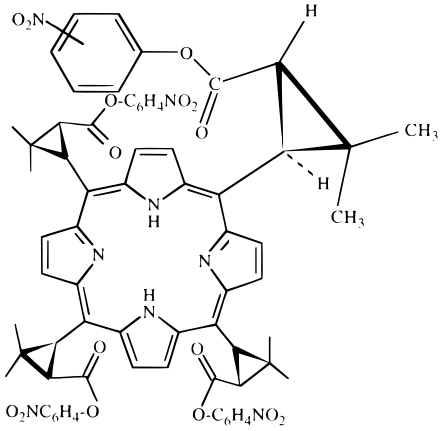
Metal complexes that drastically alter their shape upon binding of a ligand are not very common,[1,2] and very few have been fully characterized by X-ray structure determinations of both conformers. We report on an "open" zinc porphyrin host molecule that swings into a "closed" form upon binding a pyridine base. This conformational flip, which is reversible, is based on a rotation of the porphyrin substituents around their bonds to the *meso* positions; the X-ray structures of the two conformers show that it optimizes complementarity between host and guest (induced fit[3]). The description of this system as a pyridine-sensitive Venus flytrap[1,4] porphyrin readily comes to mind in view of its conceptual similarity to the insectivorous plant *Dionaea muscipula*.

The industrially available chiral cyclopropane derivative 1(*R*)-*cis*-hemicaronaldehyde[5] ("biocartol") is a convenient source of low symmetry (C_2) metal complexes of tetramethylchiroporphyrin (H_2TMCP), which are useful prototypes of asymmetric catalysts and enantioselective receptors.[1,6] In the view of promoting attractive $\pi-\pi$ interactions[1,7] between ester substituents and aromatic ligands, the *m*- and *p*-nitrophenyl esters of 1(*R*)-*cis*-caronaldehydic acid were synthesized[8] and condensed with pyrrole to afford the corresponding tetra-*m(p)*-nitrophenylchiroporphyrins H_2T-*m*-NPCP (**1**) and H_2T-*p*-NPCP (**2**) in 5−10% yield, (Figure S1, Supporting Information). In both cases, this atroposelective cyclization affords the $\alpha\beta\alpha\beta$ atropisomer as the sole porphyrin product. The latter is then smoothly converted to its zinc complex, [Zn(EtOH)(T-*m*-NPCP)] (**3**) or [Zn(EtOH)(T-*p*-NPCP)] (**4**), respectively,[9] by reaction with zinc acetate in refluxing chloroform−ethanol (1:1). No atropisomerization occurs under these conditions, indicating that the bulky cyclopropyl groups prohibit rotation of the *meso* substituents.



The crystal structure of **3**[10] confirms the open conformation and the C_2 symmetry with the 2-fold axis running through the mean plane of the highly ruffled porphyrin (Figure 1 and Figure S2, Supporting Information). The zinc center and its ethanol axial ligand are therefore disordered over two equivalent positions. In addition, there are two different ethanol conformers for each position. The ethanol oxygen atom is at a long hydrogen-bonding distance to the carbonyl group. The conformation of the ester groups is such that the four carbonyl oxygen atoms are in positions nearly eclipsing the four α pyrrole carbon atoms C(a2), C(a3), C(a3)′, and C(a2)′, thereby pushing the *m*-nitrophenyl groups to the periphery of the porphyrin and nearly perpendicular to its mean plane. The similarity of ^{1}H NMR spectra for **3** and **4**, and particularly the absence of a notable porphyrin ring current effect on the phenyl resonances, suggests analogous conformations of the nitrophenyl ester groups of **3** and **4** in solution.

Addition of an equivalent of 3,5-lutidine to a $CDCl_3$ solution of **4** results in an immediate and complete switching from the open $\alpha\beta\alpha\beta$ conformation to the closed, axially ligated $\alpha\alpha\alpha\alpha$ form (Figure S3, Supporting Information). This flipping is conveniently monitored by the change of multiplicity of the pyrrolic proton NMR resonances from a D_2-symmetric to a C_4-symmetric pattern[11] (Figures S4−S7, Supporting Information). Pyridine, 4-methylpyridine, and piperidine all induce a qualitatively similar effect, but the conversion to the closed form is incomplete and the $\alpha\alpha\alpha\beta$ atropisomer is formed as well to varying degrees (Table 1). Addition of hydrochloric acid to a solution of the closed $\alpha\alpha\alpha\alpha$ conformer opens the flytrap, affording the $\alpha\beta\alpha\beta$ atropisomer. Crystals of X-ray quality were obtained by diffusion of pyridine into a solution of **4** at room temperature. The pyridine adduct [Zn(py)(T-*p*-NPCP)] (**5**) exhibits the $\alpha\alpha\alpha\alpha$ conformation (Figure 2 and Figure S8, Supporting Information). Its unusual stereochemical features give a clue to the origin of this conformational switching. The porphyrin macrocycle is highly C_{4v} domed, and the plane of the pyridine ligand is in eclipsed orientation with a N−Zn−N axis. The coordinated pyridine is tightly sandwiched between

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(9) Synthetic, spectroscopic, and crystallographic information is provided in the Supporting Information.

(10) Crystal data for [**3**]·1.02CH_2Cl_2: orthorhombic, space group $P2_12_12$, a = 20.6871(11) Å, b = 13.8718(14) Å, c = 12.3315(9) Å, V = 3538.9(4) Å^3, and Z = 2; 26 031 reflections were collected and appropriately averaged,[9] 9263 of which were unique (130 K, 2.21° < θ < 29.87°); 7953 reflections [$I > 2\sigma(I)$] yield R = 0.0661 and R_w = 0.1866. *Note*: the ideal formula is [**3**]·2.0CH_2Cl_2 and the total population of the solvent sites accidentally is very near one, as the two sites are effectively together only half-filled. Crystal data for [**5**]·2.71CH_2Cl_2: monoclinic, space group $P2_1$, a = 15.065(2) Å, b = 13.986(1) Å, c = 17.565(3) Å, β = 101.590(7)°, V = 3625.5(8) Å^3, and Z = 2; 27 411 reflections were collected and appropriately averaged,[9] 12 530 of which were unique (127 K, 2.18° < θ < 29.85°); 10 963 reflections [$I > 2\sigma(I)$] yield R = 0.055 12 and R_w = 0.1299. *Note*: the ideal formula is [**5**]·3.0CH_2Cl_2 and the refined 2.72 population of the solvent sites reflects an attempt to properly account for partially occupied solvent sites.
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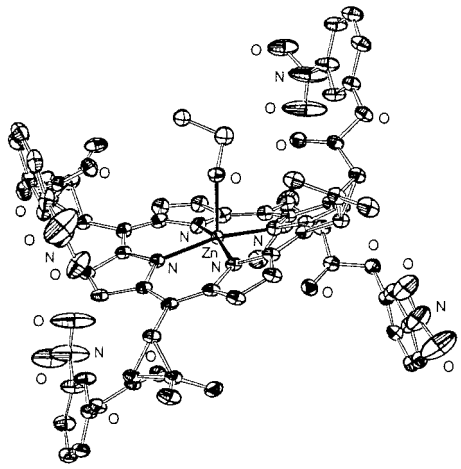

Figure 1. ORTEP view (50% probability) of the X-ray structure of the zinc chiroporphyrin [Zn(EtOH)(T-*m*-NPCP)] **3** showing the $\alpha\beta\alpha\beta$ conformation of the host in the presence of the ethanol guest.

Table 1. Atropisomer Ratios Obtained by Flipping of the Zinc Chiroporphyrin Host [Zn(L)(T-*p*-NPCP)] in the Presence of 10 equiv of Guest L in Deuterated Chloroform Solution

L	3,5-lutidine	4-methylpyridine	pyridine	piperidine
$\alpha\alpha\alpha\alpha/\alpha\beta\alpha\beta$	>100	2.0	1.2	0.6
$\alpha\alpha\alpha\beta/\alpha\beta\alpha\beta$	n.d.[a]	1.1	0.8	n.d.[b]

[a] Not determined due to low accuracy. [b] Not determined due to overlapping peaks.

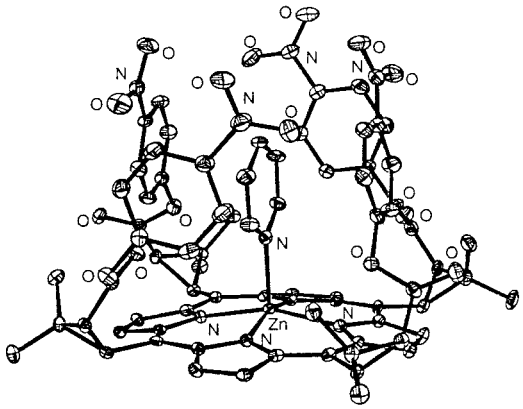

Figure 2. ORTEP view (50% probability) of the X-ray structure of the zinc chiroporphyrin [Zn(py)(T-*p*-NPCP)] **5** showing the $\alpha\alpha\alpha\alpha$ conformation of the host in the presence of the pyridine guest. The coordinated pyridine is tightly sandwiched between a pair of nearly parallel *p*-nitrophenyl groups by double face-to-face $\pi-\pi$ stacking, while the other pair is nearly perpendicular and exhibits edge-to-face interactions with it.

a pair of nearly parallel *p*-nitrophenyl groups by double $\pi-\pi$ stacking ($d_{\text{center-center}} = ca.$ 3.5 Å), while the other pair is nearly perpendicular and exhibits edge-to-face interactions with it ($d_{\text{center-center}} = 5.0$ and 5.5 Å). A single carbonyl group, C(16)−O(1), shows the usual "inward" orientation, while the other three are directed radially outward.

The energy landscape revealed by molecular mechanics calculations is very complex, but some general conclusions can be drawn. The macrocycles of the $\alpha\alpha\alpha\alpha$ conformers are predominantly domed and the $\alpha\beta\alpha\beta$ conformers are predominantly ruffled, in agreement with the crystal structures. For the pyridine complex, the lowest-energy $\alpha\alpha\alpha\alpha$ conformer for any specific arrangement of the carbonyls is always lower in energy (*ca.* 1 kcal/mol) than the corresponding $\alpha\beta\alpha\beta$ conformer. This energy gain provides a plausible driving force for the $\alpha\beta\alpha\beta \rightarrow \alpha\alpha\alpha\alpha$ atropisomer conversion. In contrast, for the ethanol complex, the $\alpha\beta\alpha\beta$ conformer is more stable (by *ca.* 2 kcal/mol) than the $\alpha\alpha\alpha\alpha$ conformer. The preference of these ligands for either conformer is probably the combined effect of (a) a minimization of the steric repulsion between the substituents and the axial ligand and (b) a maximization of their attractive van der Waals interactions by favorable packing. The predicted preference of ethanol and pyridine for a particular conformer is carried over into the crystal environment. Structural decomposition of both the calculated and X-ray structures of the pyridine complex into contributions from ruffling, saddling, doming, and waving distortions[12] shows that the macrocycle is almost purely domed. This domed conformation also favors the eclipsed ligand orientation which is observed in the crystal structure.

The apparent lower rotation barrier of the porphyrin substituents in the presence of pyridine bases deserves further investigation. Our current interpretation, based on the crystal structures, is that the highly domed conformation of the porphyrin, which results from strong binding of pyridine (Zn−N = 2.119 Å) allows fast *meso* group rotation at room temperature and attainment of a dynamic equilibrium between atropisomers. In contrast, weak ethanol ligation results in a long Zn−O bond (2.227 Å) and in a ruffled porphyrin conformation which inhibits *meso* group rotation. Molecular mechanics calculations provide significantly lower estimates for the $\alpha\alpha\alpha\alpha \rightarrow \alpha\alpha\alpha\beta$ rotation barrier of the domed porphyrin complex (26−35 kcal/mol) than for the $\alpha\beta\alpha\beta \rightarrow \alpha\alpha\alpha\beta$ transition of the ruffled conformer (30−45 kcal/mol).

It is noteworthy that the degree of flipping induced by pyridine and its derivatives parallels their substituent electron-releasing properties (3,5-lutidine > 4-methylpyridine > pyridine), in keeping with the electrostatic component of $\pi-\pi$ interaction and the known electron donor−acceptor arene complexation chemistry.[1,13] The flipping ability of the host substituents (*p*-nitrophenyl > *m*-nitrophenyl) follows the same trend. On the other hand, the lower effect of piperidine (pyridine > piperidine) is likely to reflect a less-than-ideal fit of this guest in a chair conformation relative to the flat aromatic core of pyridine. The observed ranking of guests suggests that the driving force for the $\alpha\beta\alpha\beta \rightarrow \alpha\alpha\alpha\alpha$ conversion is enthalpic (the entropic change is similar) and arises from more favorable interactions between host and guest.

We note that the ligand-triggered $\alpha\beta\alpha\beta \leftrightarrow \alpha\alpha\alpha\alpha$ conversion could in principle bring together and align appropriate reactive or catalytic groups, as well as provide a mechanism for the controlled delivery of pyridine-containing drugs. Its utility in the creation of shape-selective and chiral oxygenation catalysts, and of hemoprotein analogues, will also be explored.

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Supporting Information Available: Synthetic schemes for **1** and **2**, 400 MHz ^{1}H NMR spectra of **4** and of **4** in the presence of 1 equiv of 3,5-lutidine, and X-ray structural information on **3** and **5** (54 pages). An X-ray crystallographic file, in CIF format, is available through the Internet only. See any current masthead page for ordering and Internet access instructions.

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