Structural Evidence for Nonplanar Keto- and Planar Enol-forms of Oxophlorins

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The first structural investigation of a zinc(II) and a free-base oxophlorin reveals considerable conformational differences between the keto- (**1**) and enol-form (**2**) of oxophlorins.

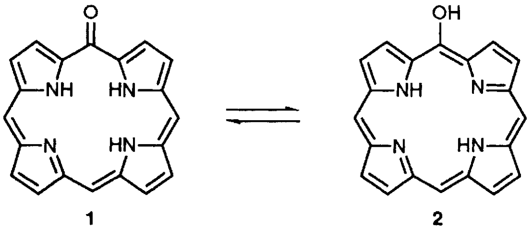
Oxophlorins have been postulated as intermediates in the catabolism of porphyrins leading to bile pigments.[1] While the chemistry of these compounds has been elucidated in detail, structural information on oxophlorins is rare.[2–4] One of the most intriguing properties of the oxophlorins is the possibility of keto–enol tautomerism.[5] The free bases have the ketonic structure **1** while the enolic tautomer **2** is found in several derivatives such as metallo(II) derivatives and enolic esters. For metallo complexes with trivalent metal ions the keto form has been suggested.[5,6]

Tetrapyrroles are currently under active scrutiny with respect to protein–chromophore interactions. Different conformations of the same chromophore are believed to be responsible for different functions with associated changes in their physicochemical properties.[7] Oxophlorins represent an intriguing example of a molecular switch since the keto-form suggests a considerably altered conformation when compared with porphyrins.

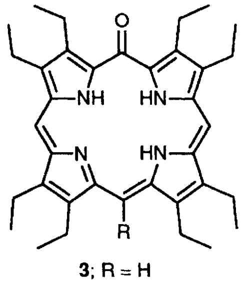
Fig. 1 shows the molecular structure of (2,3,7,8,12,13,17,18-octaethyloxophlorinato)zinc(II) **Zn3**.† The compound crystallized as the pyridine adduct with the zinc atom situated on a crystallographic inversion point; the central macrocycle is essentially planar. The planar structure and the spectroscopic properties strongly suggest that this compound has a 'porphyrin-type' macrocycle, which requires the enol form of the oxophlorin. The average bond lenths of 2.083(2) Å for Zn–N(pyrrole) and of 2.347(2) Å for Zn–N(pyridine) are in good agreement with those found in the pyridine adduct of zinc(II) octaethylporphyrin.[8] This similarity in the conformational parameters also points to a porphyrin-type structure. Unfortunately the highly symmetric molecule has a considerable degree of rotational freedom in the crystal. This leads to a disordering of the oxo-function over two positions (0.54 and 0.46 occupancy, each) which gives an almost statistical distribution of the oxo-group over the four *meso*-positions; thus, no detailed analysis of the bond order is possible. Previous literature has shown[9a] that zinc(II) oxophlorins, *e.g.* **Zn3**, can exist in solution as the neutral free radical. Very recent work has concluded[9b] that this is true also for the crystalline state of **Zn3**, though this cannot be determined directly from our own structure (Fig. 1).

In order to establish clearly the conformational features of the oxophlorins and to circumvent the rotational disordering observed in the zinc–octaethyl derivative we decided to use porphyrin derivatives with additional substituents which might act as an 'anchor' for the tetrapyrrole in the crystal. During studies on the nucleophilic substitution in π-cation radicals of *meso*-substituted porphyrins it was shown that zinc(II) oxophlorins react with thallium(III) trifluoroacetate followed by work up in the presence of nucleophiles to give the 5,15-disubstituted products.[10] Compounds of this type seemed to be asymmetric enough to prevent the above mentioned disordering phenomenon.

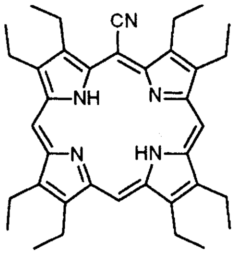
Fig. 2 shows the molecular structure of 15-cyano-2,3,7,8,12,13,17,18-octaethyl-5-oxophlorin **4**.‡ The molecule is clearly non-planar and shows a severe saddle-shaped conformation. The average deviation from the mean plane of the macrocycle is 0.29 Å with the *meso*-carbon atoms alternately displaced 0.39 Å above and below the mean plane. The individual pyrrole rings are tilted with respect to the mean plane by 18.5, 27.5, 8.9 and 19.3°. Neighbouring pyrroles are tilted by 42.1, 25.8, 20.5 and 21.7°, with respect to each other.



1 **2**



3; R = H
4; R = CN



5

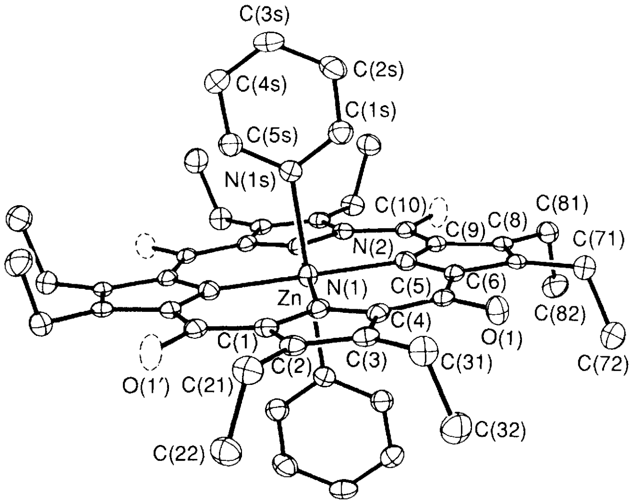


Fig. 1 The molecular structure of **Zn3**. Ellipsoids are drawn for 50% occupancy. Hydrogen atoms have been omitted for clarity. Dashed circles indicate the disordered positions for the oxygen atom.

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† *Crystal data* for **Zn3**: dark red parallelpipeds from CH_2Cl_2–MeOH (1% pyridine), $C_{36}H_{43}N_4OZn{\cdot}(C_5H_5N)$, triclinic $P\bar{1}$, 120 K, Cu-Kα, a = 9.904(3), b = 10.273(2), c = 10.472(2) Å, α = 80.04(2), β = 890.43(2), γ = 66.35(2)°, V = 959.2 Å^3, R = 0.036.

‡ *Crystal data* for **4**: small blue crystals from CH_2Cl_2–n-hexane, $C_{37}H_{45}N_5O{\cdot}2CH_2Cl_2$, monoclinic $P2_1/c$, 120 K, Cu-Kα, a = 13.696(4), b = 18.732(8), c = 15.416(7) Å, β = 105.88(2)°, V = 3804.1 Å^3, 2651 observed reflections with $I > 3.5\sigma(I)$, R = 0.118. Severely disordered molecules of solvation that could not be modelled satisfactory. The analysis of better crystals is currently under way.

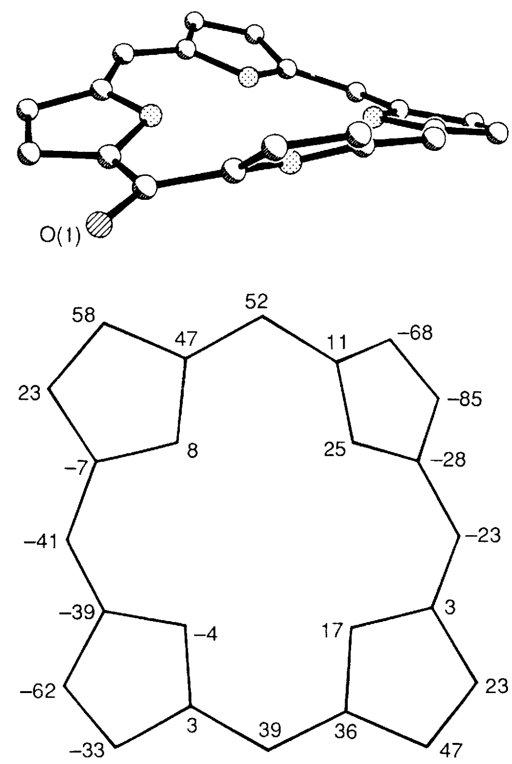

Fig. 2 The molecular structure of **4**. Hydrogen atoms and side groups have been omitted for clarity. The lower figure shows the deviations from the least-square plane of the 24 macrocycle atoms (Å × 10^2).

In order to establish that the conformational distortion is indeed due to the keto character of the oxophlorin and the interruption in the conjugated system and not due to steric effects of the cyano group the respective 5-cyanooctaethylporphyrin **5** was also investigated.§ The molecule is planar, with a mean deviation from the least-square plane of the porphinato core of 0.025 Å (data not shown). The conformational distortion can therefore be attributed solely to the carbonyl group and to a small extent to packing forces introduced by neighbouring molecules of solvation (n-hexane). The asymmetry in the distortion might be attributed to steric interaction of the three hydrogen atoms in the tetrapyrrole core. The C–O bond length is 1.233(15) Å and indicates clearly the double bond character. The C_α–C_m–C_α angle for the oxo-substituted position-5 is 121.4° while the other three *meso*-positions exhibit an average value of 127.2°. A smaller value for the carbonyl-type *meso*-positions opposed to the unsubstituted *meso*-positions 10 and 20 was also observed in the structure of a 5,15-dioxoporphodimethene, a related compound with two carbonyl groups at opposite *meso*-functions.[11]

The severe distortion of the keto form of the oxophlorins make these compounds interesting ligands for further studies on metal coordination with unusual geometry and catalytic activity of tetrapyrroles and also explains the very different optical spectra observed for the keto- and enol-forms.[3,5] Biologically, the switch between keto- and enol-form, with the saddle-shaped conformation of the former, might activate the iron porphyrin system for breakdown to the bile pigments.

We are currently investigating these compounds in more detail to establish their solution structure and to study the effect of different metals and axial ligands on their conformation.

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§ *Crystal data* for **5**: $C_{37}H_{45}N_5$, monoclinic $P2_1/n$, 120 K, Cu-Kα, a = 15.704(3), b = 9.122(2), c = 21.806(4) Å, β = 95.15(1)° V = 3111.1 Å^3, R = 0.102.

Atomic coordinates, bond lengths and angles, and thermal parameters for **Zn3**, **4** and **5** have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

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