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[26]Hexaphyrin(1.1.1.1.0.0): an all-aza isomer of rubyrin with an inverted pyrrole subunit

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The synthesis, characterization and X-ray structure of an hexapyrrolic macrocycle, [26]hexaphyrin(1.1.1.1.0.0), is reported; it is characterized by a partially inverted structure.

Expanded porphyrins continue to attract attention as synthetic targets due to the fact that they often display features, such as anion binding and neutral substrate recognition, that are not seen in normal porphyrins.[1–3] Recently, a special structural feature, namely the inversion of one or two of the pyrrolic-subunits has been observed in certain expanded porphyrins. For instance, the free-base form of *meso*-tetraphenylsapphyrin exhibits such an inverted structure. Upon bis-protonation, however, this species undergoes a change in conformation adopting a 'regular' planar structure wherein all the nitrogens are pointed inward.[4,5] Similar structural features have been observed for certain heteroatom-containing *meso*-tetraphenylsapphyrins;[6–8] depending on the protonation state and the nature of the heteroatom, these latter systems can exhibit either an inverted or a planar structure. Several heterorubyrins (*e.g.* **1** with X = S or Se, respectively) have also been found to adopt bis-inverted conformations under appropriate conditions.[7] Another recent report described the isolation of a novel [26]hexaphyrin(1.1.1.1.1.1) in low yield as a side product in the Rothemund synthesis of porphyrins,[9] that exhibits a bis-inverted structure in its free-base form. In this instance, the influence of protonation has yet to be established. Interestingly, the original [26]hexaphyrin(1.1.1.1.1.1), first reported by Gossauer in 1983,[10] was found to adopt a different conformation. Rather than existing in a form wherein one or more of the pyrrolic subunits is inverted, this system, bearing substituents on the β-pyrrolic but not *meso*-carbon positions, was found to adopt a conformation wherein the two opposing *meso*-C*H* protons point inward. Upon metalation with $PdCl_2$, however, it is believed that this latter hexaphyrin, never characterized structurally, rearranges such that two of the six pyrrolic subunits point outwards.[11] The subtle nature of the conformational effects evident in hexapyrrolic macrocycles and their structural origins are currently far from understood. They thus provide an impetus for further study. In this communication we report the synthesis of the hitherto unknown hexapyrrolic macrocycle, [26]hexaphyrin(1.1.1.1.0.0) (**2**). Based on an analysis of molecular models, this particular system was expected to adopt a conformation wherein one pyrrolic subunit (only) is inverted.

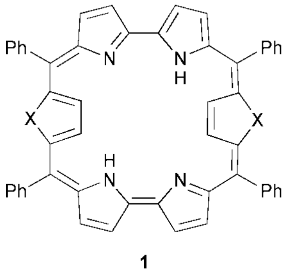
The synthesis of compound **2** is summarized in Scheme 1. Briefly, it is obtained in 46% yield from the acid catalyzed condensation of a 1 : 1 mixture of the diphenyltripyrane **3**[12] with the diformylhexamethylterpyrrole **4**.[13]

[26]Hexaphyrin(1.1.1.1.0.0) (**2**) constitutes the first true isomer of rubyrin.[14] While other porphyrin analogues bearing the same combination of four *meso*-like carbon atoms and six heterocyclic subunits are known, in particular the bronzaphyrins,[15] in all cases at least one of the six pyrrolic units present in rubyrin has been replaced by a furan or a thiophene.†

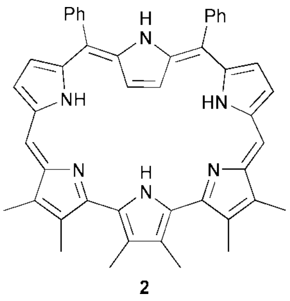
Macrocycle **2** is aromatic as judged from the ^1H NMR (d_6-DMSO) spectra of the protonated and free-base forms, respectively. The dihydrochloride salt, $H_2\mathbf{2}^{2+}\cdot 2Cl^-$, in particular, shows a strong magnetic ring current effect. Here, upfield shifts for the inner N*H* protons are found, with resonances observed at −0.75, −0.14 and 0.05 ppm in a 1 : 2 : 2 ratio. One more upfield resonance, namely at −2 ppm is also observed. On the basis of a two-dimensional C–H correlation experiment, this signal is ascribed to a C*H* proton. Indeed, the upfield position of this resonance is considered *prima facie* evidence for the inverted nature of $H_2\mathbf{2}^{2+}\cdot 2Cl^-$.‡

The COSY spectrum of **2** shows a correlation between the peak at −2 ppm with one at 15 ppm, a signal that was found to correspond to the outer N*H* proton. The $\Delta\delta$-value of 17 ppm between these two signals provides strong support for the aromatic nature of the inverted macrocycle. Also, the C*H* protons of the *meso*-positions were found to resonate at 11.4 ppm while two doublets at 9.2 and 9.8 ppm, respectively, were found to correspond to the two outer β-pyrrole C*H* protons. Interestingly, in the ^1H NMR spectrum of the free-base macrocycle **2** the $\Delta\delta$-value between the β-C*H* protons of the inverted pyrrole (δ = 3.5 ppm) and the N*H* signal (δ = 9.8 ppm) of the same pyrrole is reduced to 6.3 ppm. The C*H* protons of the *meso*-positions resonate at 8.5 and the two doublets which correspond to the two outer β-pyrrole C*H* protons are shifted to 7.3 and 8 ppm, respectively. The reduced aromatic effect for the free-base form of macrocycle **2** can be rationalized in terms of a lower number of fully conjugated π-electron peripheries (*i.e.* fewer aromatic resonance structures can be drawn). It is also possible that **2** is subject to a greater distortion from planarity than $H_2\mathbf{2}^{2+}\cdot 2Cl^-$. Nevertheless, the critical point is that **2** is still considered to be inverted; the $\Delta\delta$-value between the outer and inner β-C*H* protons amounts to 5 ppm as the result of an extant but weak ring current effect.

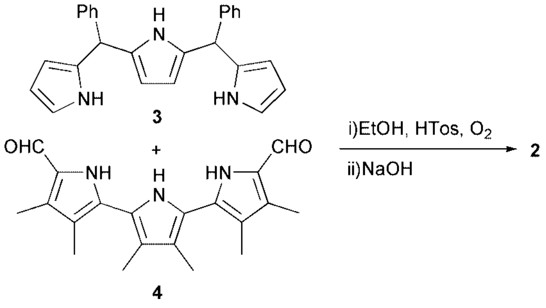
The NOESY spectrum supports the assignment of an inverted structure to the free-base form of **2**. A correlation is found



1



2



Scheme 1

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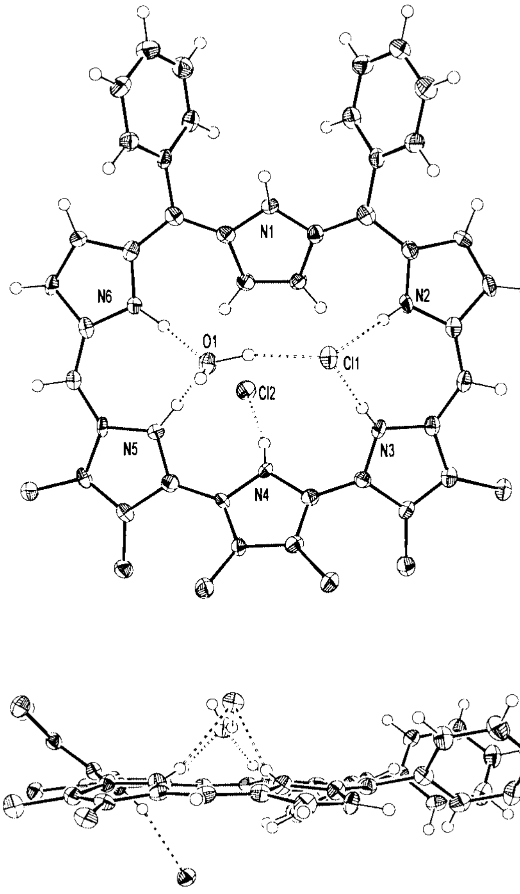

Fig. 1 Top and side views[16] of $H_2\mathbf{2}^{2+}\cdot 2Cl^-$ with a partial atom labeling scheme. Thermal ellipsoids are scaled to the 50% probability level. Hydrogen atoms shown are drawn to an arbitrary scale. Dashed lines are indicative of a hydrogen bonding interaction.

between the β-C*H* protons of the inverted pyrrole with the N*H* proton of the middle pyrrole of the terpyrrole subunit. Additionally, the outer N*H* proton clearly interacts with the *ortho-H* protons of the *meso*-phenyl substituents, findings which can only be rationalized in terms of an inverted structure. The UV-vis spectra of **2** and $H_2\mathbf{2}^{2+}\cdot 2Cl^-$ support the assumption that the free-base form of **2** is subject to a greater deviation from planarity than its bishydrochloride salt, $H_2\mathbf{2}^{2+}\cdot 2Cl^-$. In particular the extinction coefficients are found to be reduced by a factor of 2–2.5 in the case of the free-base.§

Definitive proof for the inverted nature of $H_2\mathbf{2}^{2+}\cdot 2Cl^-$ was obtained from a single crystal X-ray diffraction analysis. The resultant structure is shown in Fig. 1.¶ In addition to the two bound chloride counteranions, there is one molecule of water incorporated into the structure. Several hydrogen bonding interactions, indicated by dashed lines, are found between the pyrrolic N*H* protons and the water and the chloride anions, respectively. These might, at least to some extent, account for the partial deviation from planarity. Another hydrogen bonding interaction is found between the water and a molecule of tetrahydrofuran (not shown).¶ The middle pyrrole of the terpyrrole subunit is tilted out of the plane, minimizing the interactions between the β-methyl groups.

In summary, the approach reported here provides an easy, high-yielding access to a new class of rubyrin analogue, namely [26]hexaphyrin(1.1.1.1.0.0) (**2**). This new macrocycle differs quite dramatically from its better studied parent system. Not only is one pyrrole-unit found to be inverted in the case of **2**, this prototypical [26]hexaphyrin(1.1.1.1.0.0) is also found to be stable in both its free-base and protonated forms. Rubyrin, on the other hand, is stable only in its bisprotonated form.[14] That the middle pyrrole of the tripyrrane subunit of **2** remains inverted in both these states is interesting, especially in light of the behavior of sapphyrins. In these latter pentapyrrolic systems, the pyrrole unit may be either 'inverted' or 'normal', depending on conditions, substitution paterns and the nature of the heteroatom contained within the central heterocycle of the constituent tripyrrane-subunit. In fact, **2** can be thought of as an 'expanded sapphyrin' with the bipyrrolic subunit exchanged for a terpyrrole. In this context it is worth highlighting the fact that **2** displays a greater propensity for inversion when fully protonated than does tetraphenylsapphyrin. Indeed, this latter species is found to adopt a planar, pyrrole-in conformation when fully protonated.[4,5] These disparities underscore the richness of structural space that may be sampled through the construction of appropriately designed new expanded porphyrin systems.

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Notes and references

† In a more systematic sense, rubyrin might be referred to as [26]hexaphyrin(1.1.0.1.1.0) while bronzaphyrin is a [26]hexaphyrin(2.0.0.2.0.0).

‡ Such behavior has been reported for N-confused porphyrins where 'inversion' is enforced.[17,18]

§ UV-vis (CH_2Cl_2) λ_{max} (nm) (ε in mol^{-1}·l^{-1}) of **2**: 502 (61100), 531 (73400), 782 (20200); $H_2\mathbf{2}^{2+}\cdot 2Cl^-$: 533 (173000), 556 (156000), 733 (10400), 877 (30200).

¶ Crystallographic summary for $(C_{46}H_{42}N_6)^{2+}\cdot 2Cl^-\cdot 2C_4H_8O\cdot H_2O$: Crystals were grown by layering a CH_2Cl_2 solution of $H_2\mathbf{2}^{2+}\cdot 2Cl^-$ with THF. Small, very dark prisms, monoclinic, $P2_1/c$, μ = 0.189 mm^{-1}, Z = 4 in a cell of dimensions: a = 20.6415(5), b = 13.3094(4), c = 17.2658(8) Å, β = 95.591(2)°, V = 4720.8(3)Å^3, ρ_{calc} = 1.28 g cm^{-3}, F(000) = 1936. A total of 8152 unique reflections were measured on a Nonius Kappa CCD using graphite monochromatized Mo-Kα radiation (λ = 0.71073Å) at −150 °C. The structure was refined on F^2 to an R_w = 0.184, with a conventional R = 0.0983 (5669 reflections with $F_o > 4[\sigma(F_o)]$), and a goodness of fit = 1.19 for 574 refined parameters using the SHELX-97 package.[19] Two molecules of THF were observed in the unit cell, one of which was severely disordered. The contribution to the data by this molecule was removed using the utility SQUEEZE, found in PLATON98.[20] CCDC 182/1704. See: http://www.rsc.org/suppdata/cc/b0/b003777j/ for crystallographic data in .cif format.

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