ChemComm

Cite this: *Chem. Commun.*, 2011, **47**, 6813–6815

www.rsc.org/chemcomm

COMMUNICATION

Conformational and spectroscopic properties of π-extended, bipyrrole-fused rubyrin and sapphyrin derivatives†

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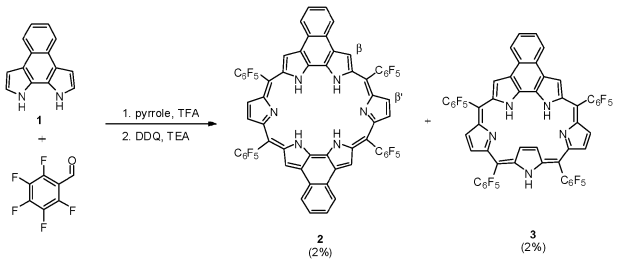
Received 26th March 2011, Accepted 4th May 2011
DOI: 10.1039/c1cc11733e

Two new expanded porphyrins, naphthorubyrin and naphthosapphyrin, were synthesized. The π-extended rubyrin was isolated and structurally characterized in its monoprotonated form. The sapphyrin congener undergoes pyrrole inversion as a function of the protonation state. These conformational effects are reflected in the spectroscopic features, including the excited singlet state lifetimes.

Expanded porphyrins are pyrrole-containing macrocyclic compounds that contain more than 16 non-hydrogen atoms in their innermost periphery. This class of compounds includes a variety of cyclic systems with more than four pyrrole rings linked in a conjugated fashion. The interest in these latter systems lies in their potential applications in various fields including anion recognition,[1] photodynamic therapy (PDT),[2] and MRI contrast agent development.[3] Expanded porphyrins have also attracted attention as nonlinear optical materials and as systems with which to explore the subtleties of aromaticity.[4] In recent years, many expanded porphyrins and their analogs have been reported in the literature.[5] Among them, two systems, namely the penta- and hexapyrrolic expanded porphyrins, sapphyrin and rubyrin, are of particular interest because of the historic role they played in the initial development of porphyrin analogue chemistry. These systems and their heterocyclic analogues (where one or more pyrroles is replaced by a different heterocycle) exhibit a considerable degree of structural diversity, as well as unique spectroscopic features.[6] Certain sapphyrins and rubyrins are also known to show conformational motion, undergoing in particular "pyrrole inversion" such that one or more of the constituent pyrrole NH protons points "in towards" or "out from" from the center of the ring. In an effort to understand further the nature of this inversion process we have designed and wish to report here a new set of sapphyrin and rubyrin derivatives derived from the fused bipyrrole precursor **1** (1,10-dihydrobenzo[*e*]-pyrrolo[3,2-*g*]indole). Although several rubyrins and sapphyrins have been reported in the literature and a variety of protonation and structure-based effects on conformational motion have been noted,[6b] to the best of our knowledge, this is the first time that bipyrrole rigidification has been used in an effort to impose an intrinsic conformational restriction on this set of oligopyrrolic cores. As detailed below, we have found that this creates a rubyrin (naphthorubyrin; **2**) that retains its basic structure upon protonation, whereas it gives rise to an inverted sapphyrin (naphthosapphyrin; **3**) that undergoes two successive pyrrole-based ring inversions upon protonation.

Naphthorubyrin **2** and naphthosapphyrin **3** were synthesized *via* the mixed pyrrole–aldehyde condensation shown in Scheme 1. The key precursor, naphthobipyrrole **1**, along with pentafluorobenzaldehyde and pyrrole (molar ratio: 1 : 1 : 2) were reacted in the presence of an acid catalyst (trifluoroacetic acid) at room temperature. Following DDQ oxidation, the pyrrole-inverted rubyrin **2** and sapphyrin **3** were each obtained in *ca.* 2% yield. Although the yields are low, the two compounds were easily separated by column chromatography.

Naphthorubyrin **2** was characterized as its HCl salt by standard spectroscopic methods as well as *via* single crystal X-ray diffraction analysis.‡ The resulting structure revealed



Scheme 1 Synthesis of rubyrin **2** and the pyrrole-inverted sapphyrin **3**.

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† Electronic supplementary information (ESI) available: Synthesis, X-ray crystal data and spectroscopic data are available. CCDC 812383. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc11733e

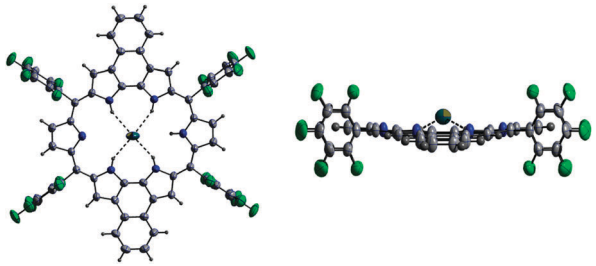


Fig. 1 Top and side views of the structure of the mono-HCl salt of naphthorubyrin **2** (**2·HCl**), as deduced from a single crystal X-ray diffraction analysis. Note that the chloride counter anion is bound within, albeit slightly above, the central core. The NH protons were seen in the difference map. H atoms are omitted for clarity in the side view. The displacement ellipsoids are scaled to the 50% probability level.

that the protonated form of this annulated rubyrin exists in a nearly planar conformation in the solid state (Fig. 1). In contrast to what might be inferred from studies of rubyrins lacking a fused bipyrrolic subunit, the HCl salt of naphthorubyrin **2** (**2·HCl**) exists as single conformation in the solid state.[6a] The central macrocyclic structure is essentially planar, and the chloride counter anion is found to be complexed within the hexaaza core. The nitrogen–chloride distances range from 3.163 Å for the four nitrogen atoms of the bipyrrole units to 3.753 Å for the two individual pyrrolic subunits. The chloride anion resides *ca.* 0.889 Å above the mean plane of the molecule.

The ^{1}H NMR spectra of the free-base, mono- and diprotonated forms of naphthorubyrin **2** were recorded in DMSO-d_6. This particular solvent was chosen because it allowed for a clean separation between all the signals. In the case of the free-base form, the β-pyrrolic proton resonances are split and appear as two singlets, whereas three distinct NH proton signals were observed upon protonation (*cf.* ESI†). Treatment with *ca.* 200 equiv. trifluoroacetic acid led to complete conversion to the diprotonated form; this species displays two NH signals in the ^{1}H NMR spectrum that are broadened compared to what is seen in the case of the monoprotonated form.

The absorption spectra of free-base rubyrin **2** recorded in CH_2Cl_2 was characterized by a split Soret band (λ_{max} = 528 and 562 nm), as well as by two Q-bands appearing at 841 and 875 nm. The mono-protonated form displayed a similar UV-vis spectrum, albeit with slightly red-shifted absorption bands. In this case, the Soret bands appeared at 532 and 590 nm while a single Q-band at 877 nm was observed. On the other hand, the diprotonated form was characterized by a relatively strong Soret-like band (λ_{max} = 557 nm), as well as by multiple Q-bands at 733, 823 and 922 nm (ESI†). The neutral and protonated forms of **2** all gave rise to appreciable fluorescence emission bands, which shift to the red on protonation (λ_{max} = 888, 908, and 948 nm for the free-base, mono- and diprotonated forms, respectively).

The free-base form of **2** (studied in toluene) shows single exponential decay dynamics with a time component of 537 ps in analogy to what is observed for normal rubyrin.[7] In contrast, the singlet excited state lifetimes of the mono- and diprotonated forms are reduced to 137 and 289 ps, respectively (ESI†). Since nonradiative deactivation processes are influenced by molecular rigidity, molecules with distorted conformations typically exhibit shorter excited state lifetimes than their corresponding planar analogues.[8] In the specific case of expanded porphyrins, considerable effort has been made to correlate conformational changes due to electronic effects or environmental factors, such as aromaticity, acidity, solvent polarity, and temperature, with various excited state properties, including singlet lifetimes, nonlinear properties, and aromaticity.[4] Moreover, structural modifications, such as pyrrole ring confusion and fusion, as well as internal (*e.g.*, intramacrocycle) linkages, have been analyzed in terms of photophysical features.[9] The excited state lifetimes recorded for the various forms of **2** are thus fully consistent with the lack of significant conformational perturbation taking place upon protonation that was inferred from the ^{1}H NMR spectroscopic analyses detailed above (ESI†).

The second product isolated from the condensation reaction shown in Scheme 1 was the pyrrole-inverted sapphyrin **3**. The existence of the inverted pyrrole subunit was inferred from the ^{1}H NMR spectrum. In particular, pyrrole NH signals at 11.04 ppm (in addition to a −0.72 ppm peak for the inner pyrrole NH protons) were observed (Fig. 2).

While the dominance of this inverted conformation stands in contrast with what was seen in the case of the naphthorubyrin **2** (*vide supra*), it is consistent with what was seen in the case of the free-base form of tetraphenyl sapphyrin. This latter species, unlike β-alkyl substituted sapphyrins, adopts a conformation wherein one pyrrole is inverted such that one constituent pyrrole NH proton faces outward from the center of the core.[10] In the case of tetraphenyl sapphyrin, protonation induces a conformational change and leads to production of a "normal" conformation wherein all three NH protons face inwards.[10] The apparent stability of this species differs from that of tetra(pentafluorophenyl)sapphyrin, where the pyrrole-inverted form has been reported as being unstable.[11]

In the case of sapphyrin **3**, two distinct sets of proton-induced changes in conformation are observed. Firstly, treatment with *ca.* 10 equiv. of trifluoroacetic acid (TFA) in $CDCl_3$ leads to changes in the ^{1}H NMR spectrum consistent with the formation of an all-in conformer (Fig. 2). In particular, the β-pyrrolic CH proton signal initially observed at −0.73 ppm was seen to shift to 8.93 ppm upon addition of 10 equiv. of

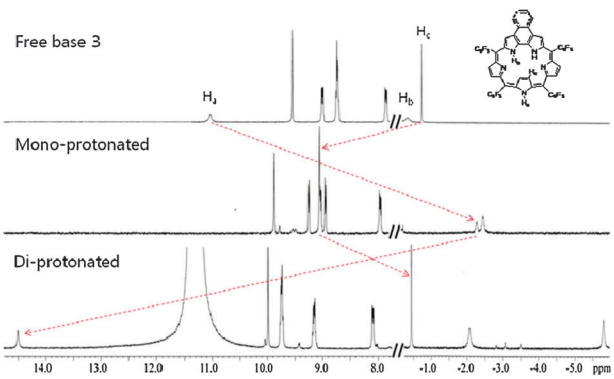
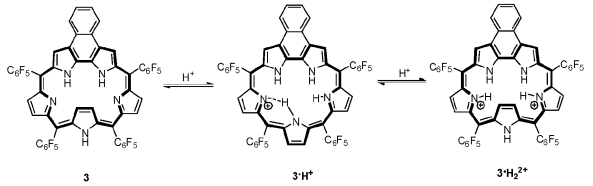


Fig. 2 ^{1}H NMR spectral changes seen for **3** upon addition of trifluoroacetic acid in $CDCl_3$. Note the proton-induced changes in the chemical shifts of the CH (H_c) and NH (H_a) protons of the pyrrole subunit undergoing inversion.



Scheme 2 Proposed conformational changes that accompany the sequential protonation of **3** with trifluoroacetic acid.

TFA, while the NH resonance originally seen at 11.04 ppm was seen to shift to −2.29 ppm. This all-in species was assigned to the mono-protonated form of **3**, $[\mathbf{3}\cdot\mathbf{H}]^+$.

The further addition of TFA led to increasing production of the diprotonated form of **3**. In the presence of *ca.* 1500 equiv. of TFA, the diprotonated form dominates. This form was characterized by features analogous to the original free-base form (Fig. 2). In particular, one set of β-pyrrolic CH resonances was seen at −0.44 ppm, while three sets of NH signals were observed (at *ca.* 14.51, −5.80, and −2.07 ppm, respectively). We thus conclude that double protonation causes re-inversion of the pyrrolic subunit and production of a "pyrrole NH out" conformation (*cf.* Scheme 2).

Proton-induced effects were also observed in the UV-vis spectrum of **3**. For instance, the free-base form of naphthosapphyrin **3** exhibits split Soret-like bands at 508 and 533 nm, along with three Q-like bands at 643, 715, and 781 nm (ESI†). In the presence of 10 equiv. of TFA where the monoprotonated form predominates, the longer wavelength absorption of the Soret-like band is shifted to 546 nm and featureless, broad Q-like bands are observed. On the other hand, the diprotonated form (obtained in the presence of excess TFA) is characterized by a reduced splitting between the two Soret-like bands and a significant increase in the molar absorptivity. Relatively clear Q-like bands are also observed at 657 and 716 nm with a rather strong feature being seen at 784 nm. There is thus a spectral congruence between the free-base and diprotonated forms of naphthosapphyrin (**3** and $[\mathbf{3}\cdot\mathbf{2H}]^{2+}$) that leads us to propose that both species have common electronic and geometric features.

Further evidence in support of the proposed protonation-dependent conformational change came from more advanced optical spectroscopic analyses of **3** in its various protonated states. While the free-base form displays a fluorescent lifetime of 1.3 ns, which is comparable to that of sapphyrin (1.2 ns; *cf.* ESI†), the excited state dynamics of the mono- and diprotonated forms show relatively reduced fluorescence lifetimes of 250 and 180 ps, respectively. In addition to these key features, short-lived components with half-lives of 33 and 14 ps are observed for the free-base and monoprotonated forms, respectively. Compared to naphthorubyrin **2**, naphthosapphyrin **3** has an asymmetric molecular structure and shorter internal distances among its pyrrolic nitrogens and inner hydrogens. It was thus considered likely that the fast time components seen for **3** and $[\mathbf{3}\cdot\mathbf{H}]^+$ reflect structural perturbations originating from the presence of the single bipyrrole-fused moiety and various internal proton transfer processes (*e.g.*, tautomerizations). In fact, transient features corresponding to the shorter time constants are seen in the case of normal sapphyrin (ESI†). The spectral features assigned to the longer time constants are thus thought to reflect the extended conjugation provided by the fused bipyrrole linkage (ESI†).

In conclusion, we have synthesized a distortion-resistant, π-extended rubyrin and a congeneric annulated sapphyrin. Naphthorubyrin **2** exhibited spectroscopic properties consistent with aromaticity and displayed a lack of conformational motion. Naphthosapphyrin **3** also displayed full aromatic character. However, in this case, one pyrrole adopts an inverted geometry. Reinversion of the inverted pyrrole was observed upon mono-protonation, while treatment with excess acid led to formation of a diprotonated form with spectral features consistent with an "NH out" arrangement of the pyrrolic subunit. These proton-triggered conformational interconversions go beyond what has been observed in other expanded porphyrin systems, including simple *meso*-tetraaryl substituted sapphyrins, and lead us to suggest that compound **3** could have a role to play as a proton-triggered molecular switching entity.

This work was supported by Basic Science Research Program through the NRF (2009-008713), the National Science Foundation (CHE 0749571 to J.L.S. and CHE 0741973 for the X-ray diffractometer), the Robert A. Welch Foundation (F-1018 to J.L.S.), and the Korean WCU program (grant R32-2010-10217-0). MEST and NRF support for the Central Instrumentation Facility at KNU and the 'Human Resource Development Center for Economic Region Leading Industry' is also acknowledged.

Notes and references

‡ Crystal data for **2·HCl** ($[C_{64}H_{20}F_{20}N_6]^{1+}Cl^-$,2($C_5H_{12}$),2($CH_2Cl_2$)): M_w = 1602.45 g mol^{-1}, size 0.25 × 0.07 × 0.05 mm, 233 K, tetragonal, $P\bar{4}2_1/m$, a = 21.411(2) Å, b = 21.411(2) Å, c = 7.5217(8) Å, $\alpha = \beta = \gamma = 90°$, V = 3448.2(7) Å^3, Z = 2, 19 139 reflections measured/1742 independent (R_{int} = 0.0938), R_1 = 0.0526, wR_2 = 0.1248 ($I > 2\sigma(I)$), R_1 = 0.0877, wR_2 = 0.1409 (all data), residual density peaks 0.318 to −0.225 e Å^3, CCDC 812383.

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