Synthesis and Structure of Non-aromatic Porphyrinoid Schiff-base Macrocycles Bearing Thiophene

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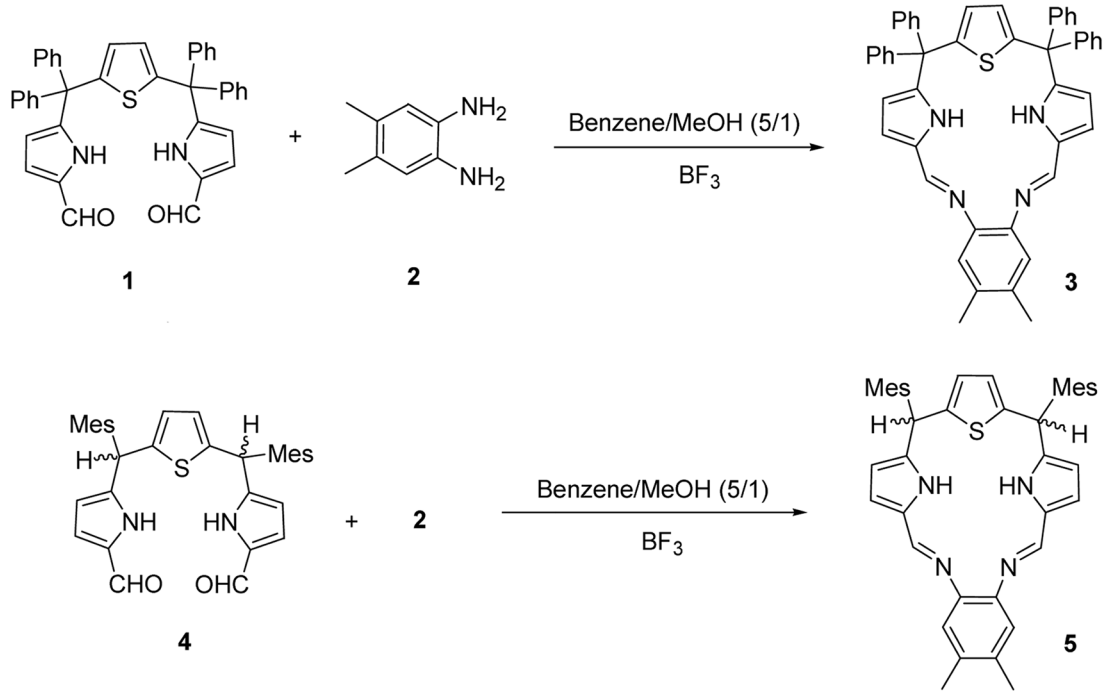
Expanded porphyrins and their metal complexes have shown considerable potentials in medicinal applications such as diagnostic or treatment tools for various deseases.[1] The hybrid macrocycles composed of the combination of part of the porphyrin and part of the Schiff-base have shown interesting physico-chemical properties. Since the report of the synthesis of fully aromatic expanded porphyrins and their metal complexes by Sessler *et al.*,[2] many new macro-aromatic porphyrinoids consisted with tripyrromethanes and imines have been synthesized and studied for potential biological applications.[3]

For example, some of the lanthanide complexes of the expanded porphyrins have been used for enhancing images in MRI[4] or for selective anion binding agents.[5] The unusual contractive cyclization accompanying with C-C bond cleavage was reported in some condensation reactions.[6,7] Here, we extend the reactions further and report the identification and solid state structure of the synthesized macrocycles.

Results and Discussions

The 1,14-bisformyl-16-thiatripyrromethane derivatives **1** was synthesized as similar way as previously reported procedure for the synthesis of **4**.[6] Then, **1** was condensed with aromatic diamine **2** in the presence of catalytic amount of $BF_3 \cdot OEt_2$ to afford the macrocycle **3** in 75% yield as shown in Scheme 1. Condensation of **4** with diamine **2** also afforded similar macrocycle **5** in relatively lower (19%) yield.[8]

In spite of the presence of easily oxidizable protons at *meso*-positions, the concomitant air oxidation was not observed during the reaction. Moreover, attempted oxidation of **5** with rather stronger oxidants such as DDQ, proton sponge or *p*-chloranil was not successful and only extensive decomposition of **5** was observed. These observations are somewhat contradictory with the results reported earlier.[8] Macrocycle **3** and **5** must be non-aromatic and the fully oxidized macrocycles must be anti-aromatic. The fact that



Scheme 1

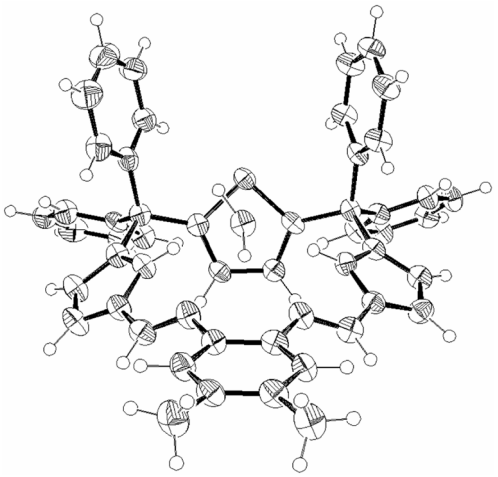


Figure 1. Solid-state structure of macrocycle **3** deduced from X-ray analysis.

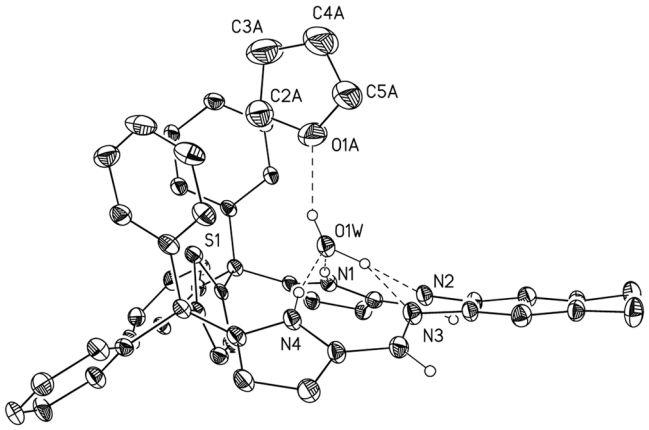


Figure 2. View of the H-bonding interactions involving **3** and the H_2O and THF molecules. Displacement ellipsoids are scaled to the 30% probability level. Most hydrogen atoms have been removed for clarity. Dashed lines are indicative of the H-bonding interactions. The geometry of these interactions are: O1W-H1WA···N2, O···N 2.955(5) Å, H···N 2.10 Å, O-H···N 141°; O1W-H1WA···N3, O···N 2.889(5) Å, H···N 2.08 Å, O-H···N 136°; O1W-H1WB···O1A, O···O 2.716(6) Å, H···O 1.90 Å, O-H···O 134°; N1-H1N···O1W, N···O 2.870(5) Å, H···O 1.98 Å, N-H···O 173°; N4-H4N···O1W, N···O 2.854(5) Å, H···O 1.97 Å, N-H···O 168°.

the resonance signals of the pyrrole NHs (δ= 7.14 ppm) and β-pyrrole-Hs (δ= 6.49 and 5.84 ppm) were appeared in the similar region of those of **1**, support this conclusion. However, the absorption spectra of **3** and **5** showed rather strong Soret-like band at 360-380 nm indicating the existence of somewhat extended conjugations in the molecule.

Synthesized macrocycle **3** was characterized by standard spectroscopic methods, as well as *via* single crystal X-ray diffraction analysis. Diffraction-grade crystals of **3** were grown by slow diffusion of hexanes into the THF/H_2O solution of the macrocycle in an atmosphere. X-ray structural analysis revealed that one solvent molecule (THF) and one water molecule are included in the unit cell and the position of the THF molecule are parallel with the two

Table 1. Hydrogen bonds for **3** [Å and °]

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
O1W-H1WB···O1A	1.03	1.90	2.716(6)	134.2
O1W-H1WA···N2	1.01	2.10	2.955(5)	140.9
O1W-H1WA···N3	1.01	2.08	2.889(5)	136.0
N1-H1N···O1W	0.90	1.98	2.870(5)	172.6
N4-H4N···O1W	0.90	1.97	2.854(5)	168.1

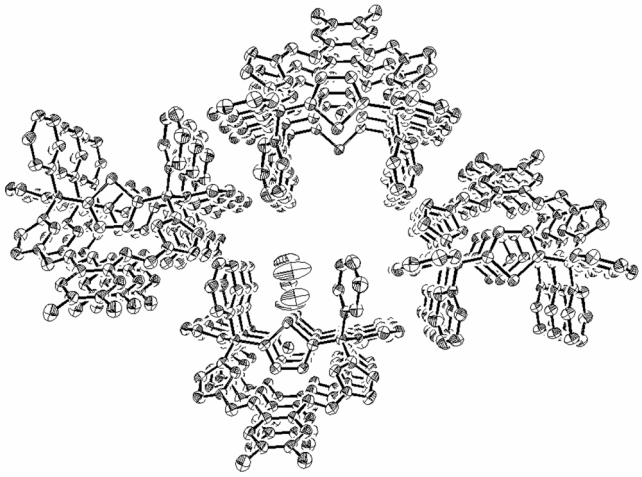


Figure 3. Crystal packing of compound **3**. The hydrogen atoms are omitted for clarity.

Table 2. Crystallographic data for the crystal **3**

Empirical formula	C_{52} H_{48} N_4 O_2 S
Formula weight	793.00
Space group	P-1
a = 9.0733(3) Å	α = 85.837(2)°.
b = 11.8905(5) Å	β = 88.319(2)°.
c = 21.3945(10) Å	γ = 70.731(2)°.
Volume	2173.08(15) Å^3
Z	2
Density (calculated)	1.212 Mg/m^3
Absorption coefficient	0.120 mm^{-1}
F(000)	840
Crystal size	0.22 × 0.19 × 0.10 mm
Completeness to theta = 25.00°	95.6 %
Data / restraints / parameters	7324 / 0 / 535
Final R indices [I > 2 sigma(I)]	R_1 = 0.0865, wR_2 = 0.1865
R indices (all data)	R_1 = 0.1494, wR_2 = 0.2127
Extinction coefficient	8.6(15) × 10^{-6}
Largest diff. peak and hole	0.637 and –0.304 e.Å^{-3}

$R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$. $wR_2 = \Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$. w = 1/[$\sigma^2(F_o)^2$ + (0.1241P)^2 + 0.000P] where P = (F_o^2+2F_c^2)/3

phenyl group at *meso*-position. The single water molecule was trapped inside the cavity through hydrogen bonding as shown in Figure 1.

The solid-state structure indicated that the two pyrrole rings and aromatic imine functions are almost planar while thiophene is oriented almost perpendicular against the

imaginary plane of the molecule. The pyrrole N-H protons bound to the oxygen atom of the trapped water *via* two NH---O hydrogen bonding interactions (Figure 2).

The pyrrolic nitrogen-to-oxygen distances are 2.906 and 2.874 Å, respectively. These hydrogen bond distances are within the ranges expected for effective hydrogen bonding interactions. The crystal packing structure showed linear stacking of oligopyrrole units and partial overlapping each other (Figure 3).

In conclusion, we have expanded the utility of '3+2' type condensation in generating Schiff-base macrocycles closely related with non-aromatic texaphyrin. The synthetic methodology described here could be applied in creating various expanded porphyrinoid macrocycles. The solid state structure indicates that the thiophene-containing macrocycle such as **3** does not possess macro-aromaticity and thiophene moiety is almost perpendicular to the imaginary mean plane of the molecule. Currently, efforts are underway to synthesize fully aromatic, core-modified expanded porphyrinoids.

Experimental Section

X-ray data were collected on a Nonius CAD4-Express diffractometer equipped with graphite-monochromated M_oK_α radiation (λ = 0.71073 Å) at room temperature. Unit cell parameters were determined from automatic centering of 25 reflections. The data were collected using the ω-2θ scan technique in the range $2.89^o < \theta < 26.27^o$. No absorption corrections were applied. The structure was solved by direct method and refined by full-matrix least-squares calculation with SHELXL-97. Anisotropic thermal parameters were used for all atoms except hydrogen. All the remaining hydrogen-atom positions were computed and refined with an overall isotropic factor in a riding model. Details on crystal and intensity data are given in Table 1 and some selected bond distances and angles are shown in Table 2.

X-ray Experimental for $C_{48}H_{38}N_4S$-H_2O-C_4H_8O. Crystals grew as pale yellow prisms by vapor diffusion of hexane into a THF solution of the macrocycle. The data crystal was cut from a cluster of intergrown crystals and had approximate dimensions; 0.22 × 0.19 × 0.10 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073 Å). A total of 259 frames of data were collected using ω-scans with a scan range of 1.1° and a counting time of 226 seconds per frame. The data were collected at 153 K using an Oxford Cryostream low temperature device. Data reduction were performed using DENZO-SMN.[1] The structure was solved by direct methods using SIR92[2] and refined by full-matrix least-squares on F2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[3] The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2 × Ueq of the attached atom (1.5 × Ueq for methyl hydrogen atoms). The hydrogen atoms on the water molecule and the pyrrole nitrogen atoms were located in a ΔF map. However, these hydrogen atoms did not refine well. Some of these atoms refined to unreasonable geometric positions or had unreasonable isotropic displacement parameters. As a result, the hydrogen atom positions on the pyrrole nitrogen atoms were idealized with an isotropic displacement parameter set to 1.2 × Ueq of the attached nitrogen atom. The hydrogen atom positions on the water molecule were obtained from the ΔF map but subsequently constrained to ride on the position of the oxygen atom of the water molecule. The isotropic displacement parameters for these two hydrogen atoms were allowed to refine without constraints. The function, $\Sigma w(|Fo|^2 - |Fc|^2)^2$, was minimized, where $w = 1/[(\sigma(Fo))^2 + (0.052*P)^2 + (3.2495*P)]$ and $P = (|Fo|^2 + 2|Fc|^2)/3$. $R_w(F^2)$ refined to 0.213, with R(F) equal to 0.0865 and a goodness of fit, S = 1.21. Definitions used for calculating R(F), $R_w(F^2)$ and the goodness of fit, S, are given below.[4] The data were corrected for secondary extinction effects. The correction takes the form: $F_{corr} = kF_c/[1 + (8.6(15) \times 10^{-6})* F_c^2 \lambda^3/(\sin 2\theta)]^{0.25}$ where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[5]

Synthesis of Macrocycle (3). To the solution of 1,14-bisformyl-5,5,10,10-tetraphenyl-16-thiatripyrromethane **1** (0.1 g, 0.17 mmol), 4,5-dimethyl-1,2-phenylenediamine (0.023 g, 0.17 mmol), benzene (50 mL) and methanol (20 mL) was added $BF_3{\cdot}OEt_2$ (0.011 mL) under nitrogen atmosphene. The whole mixture was heated for 24 h at 85 °C. Then the mixture was cooled to room temperature and neutralized by adding K_2CO_3 (20 mg). The organic layer was dried over anhyd. $NaHCO_3$ and the solvent was removed. The remaining yellow solid was recrystallized from methanol. Yield 88 mg (75%). ^{1}H NMR ($CDCl_3$) δ 8.12 (s, 2H, imine C-H), 7.27-7.25 (m, 12H, Ar-H), 7.15-7.12 (m, 8H, Ar-H), 6.90 (s, 2H, Ar-H), 6.50 (s, 2H, thiophene-H), 6.49 (d, 2H, J = 3.7 Hz, pyrrole-H), 5.84 (d, 2H, J = 3.7 Hz, pyrrole-H), 2.26 (s, 6H, Ar-CH_3), HRMS Calcd for $C_{48}H_{38}N_4S$ 702.2817, Found 703.3122(M^++1).

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$R(F) = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|\}$ for reflections with $F_o > 4(\sigma(F_o))$. $S = [\Sigma w(|F_o|^2 - |F_c|^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p is the number of refined parameters.
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