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One-Pot Synthesis of Oxidized and Reduced Heptaphyrins with Unusual TFA Binding

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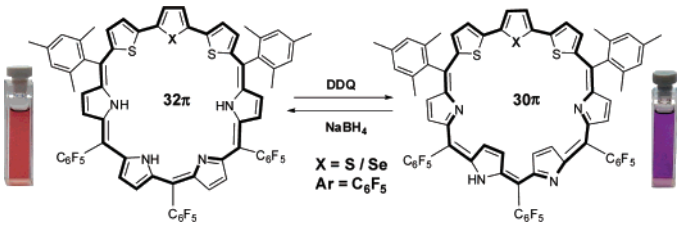
ABSTRACT



Synthesis and reversible redox interconversion between core-modified [32]heptaphyrin (1.1.1.1.1.0.0) and [30]heptaphyrin (1.1.1.1.1.0.0) are reported.

In recent years, there has been considerable effort in the development of expanded porphyrins with six or more heterocyclic rings because of their ability to exhibit a variety of interesting optical, electrochemical, stereochemical, and coordination properties (Figure 1).[1] Heptaphyrins are a class of expanded porphyrins containing seven pyrrole/heterocyclic rings connected to each other in a cyclic fashion with meso carbon bridges. Heptaphyrins adopt various conformations depending upon the number of meso bridges used for the construction of the macrocycle. For example, Sessler and co-workers reported β-substituted heptaphyrins **1** and **2**, containing two and five meso carbons, respectively. **1** turned out to be a nonaromatic 28π planar macrocycle, while **2** exhibits a "figure eight" conformation with one inverted pyrrole ring in the solid state.[2] In an earlier report from our laboratory, core-modified heptaphyrins **3** and **4**, with four and six meso carbons, exhibit planar and figure eight

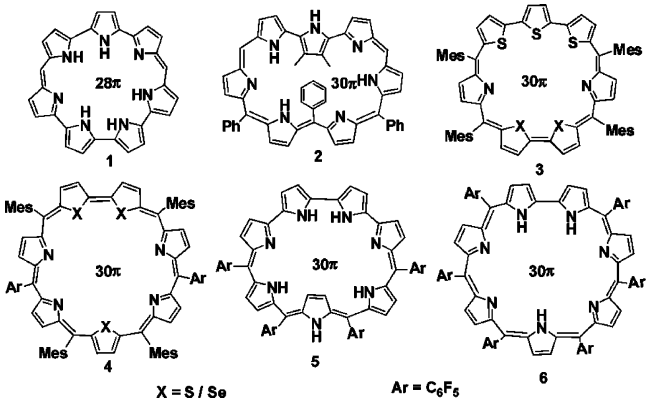


Figure 1. Heptaphyrins reported in literature.

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(1) (a) Sessler, J. L.; Gebauer, A.; Weghorn, S. J. In *The Porphyrin Handbook*; Kadish, K., Smith, K., Guilard, R., Eds.; Academic Press: San Diego, CA, 1999; Vol. 2, Chapter 9. (b) Sessler, J. L.; Gebauer, A.; Weghorn, S. J. In *Expanded Porphyrins*; Kadish, K. M., Smith, K. M., Guilard, R., Eds; Academic Press: San Diego, CA, 2000. (c) Lash. T. D. *Angew. Chem., Int. Ed.* **2000**, *39*, 1763. (d) Chandrashekar, T. K.; Venkatraman, S. *Acc. Chem. Res.* **2003**, *36*, 677. (e) Furuta, H.; Maeda, H.; Osuka, A. *Chem. Commun.* **2002**, 1795.

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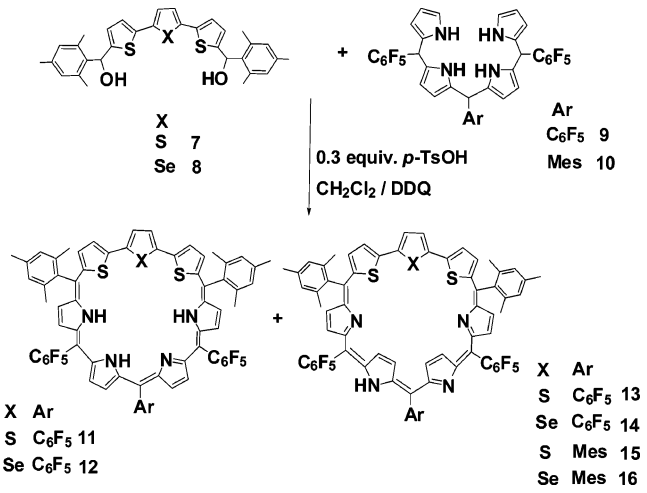
structures, respectively.[3] Recently, Osuka and co-workers reported the synthesis of heptaphyrins **5** and **6**, containing four and six meso carbons, respectively.[4] **5** in its protonated form exhibits a near planar structure with two pyrrole rings inverted, and the inverted pyrrole rings are slightly deviated from planarity. On the other hand, **6** in its protonated form has three pyrrole rings inverted, and the X-ray structure shows the inverted pyrrole ring deviates from planar conformation. From the above discussion, it is clear that the structure and conformational behavior of heptaphyrins critically depend on the number of meso carbons and the substituents present both on the meso carbons and on the pyrrole ring. In this communication, we wish to report heptaphyrins containing five meso carbon bridges and their unusual anion binding property.

We have adopted the [4 + 3] acid-catalyzed condensation reaction of terthiophene diols **7** and **8** with tetrapyrranes **9** and **10**[5,6] to synthesize a series of heptaphyrins **11**−**16**. In a typical synthesis, equimolar amounts of **7** and **9** in CH_2Cl_2 were stirred for 1 h using 0.3 equiv of *p*-toluenesulfonic acid as catalyst (Scheme 1). After oxidation with 2,3-dichloro-

Scheme 1. Synthesis of Heptaphyrins



5,6-dicyano-*p*-benzoquinone (DDQ), the products were purified by repeated basic alumina and silica gel column chromatography. Initially, a red fraction was eluted with CH_2Cl_2 and hexane (1:3). It exhibits a parent ion peak at m/z = 1306 (calcd for ($C_{69}H_{39}F_{15}N_4S_3$) [M + 1]; m/z = 1306) in the FAB mass spectrum identified as heptaphyrin **11** in 6−7% yield. After this band, a dark blue fraction was eluted with ethylacetate and CH_2Cl_2 (2:98). It exhibits a parent ion peak at m/z = 1303 (calcd for ($C_{69}H_{37}F_{15}N_4S_3$) [M+]; m/z = 1303) with 2 mass units less than **11** identified as **13** (yield 16%). **11** and **13** undergo facile oxidation and reduction.[7] For example, **11** can be quantitatively oxidized to **13** upon treatment with DDQ, while **13** can be quantitatively reduced to **11** upon treatment with $NaBH_4$. However, when tetrapyrrane-containing mesityl group **10** was used as a precursor, [30]heptaphyrins **15** and **16** were isolated.[8]

The UV/vis absorption spectra of **11** and **13** show typical nonaromatic and aromatic behavior, respectively. **11** in CH_2Cl_2 shows broad bands at 315 ($\epsilon = 0.15 \times 10^3$ M^{-1} cm^{-1}), 434 (2.4×10^3), 534 (2.1×10^3), and 749 nm (0.06×10^3), while **13** exhibits a Soret-like band at 571 nm ($\epsilon = 1.08 \times 10^5$ M^{-1} cm^{-1}) and a Q-band at 731 nm (1.5×10^4). Protonation of **11** leads to a red shift in the absorption maxima (30 nm) with 2-fold increase in the ϵ value. On the other hand, **13** has three protonation sites. Careful titration of a dilute solution of **13** with TFA leads to monoprotonation (**13H**$^+$) where the added proton attaches to the nitrogen of the inverted pyrrole. Further addition of TFA leads to simultaneous protonation of both the pyrrole rings (**13.3H**$^+$). Excess addition of TFA leads to binding of TFA through its carboxylic acid oxygen atom with pyrrole N−H···O hydrogen bonding. **13** (571 nm), **13H**$^+$ (596 nm), and **13.3H**$^+$ (613 nm) could be easily identified by their UV/vis spectrum (see Supporting Information). A typical titration of **13** with TFA at different concentrations is shown in Figure 2. The presence

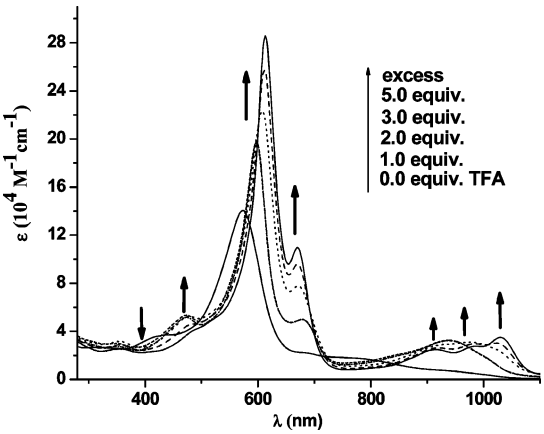


Figure 2. UV−vis spectra showing spectral changes observed upon addition of TFA to solutions of **13** in CH_2Cl_2. These are considered to reflect stepwise conversion of **13** into **13**·H$^+$[TFA]$^-$ and **13**·H$^+$[TFA]$^-$ into **13**·3H$^+$3[TFA]$^-$. The arrows indicate the direction of changes.

of isobestic points clearly suggests an equilibrium between the protonated species and the anion-bound species.

(2) (a) Sessler, J. L.; Seidel, D.; Lynch, M. *J. Am. Chem Soc*. **1999**, *121*, 11257. (b) Bucher, C.; Siedel, D.; Lynch, M.; Sessler, J. L. *Chem. Commun*. **2002**, 328.

(3) (a) Anand, V. G.; Pushpan, S. K.; Srinivasan, A.; Narayanan, S. J.; Sridevi, B.; Chandrashekar, T. K.; Roy, R.; Joshi, B. S. *Org. Lett*. **2000**, *2*, 3829. (b) Anand, V. G.; Pushpan, S. K.; Venkatraman, S.; Dey, A.; Narayanan, S. J.; Chandrashekar, T. K.; Roy, R.; Joshi, B. S.; Sastry, G. N.; Deepa, S. *J. Org. Chem*. **2002**, *67*, 6309. (c) Rath, H.; Sankar, J.; Prabhuraja, V.; Chandrashekar, T. K.; Joshi, B. S. *Org. Lett*. **2005**, *7*, 5445.

(4) (a) Hiroto, S.; Shinokobo, H.; Osuka, A. *J. Am. Chem. Soc*. **2006**, *128*, 6568. (b) Saito, S.; Osuka, A. *Chem.—Eur. J*. **2006**, *12*, 9095.

(5) Guilard, R.; Gryko, D. T.; Canard, G.; Barbe, J.-M.; Kosarna, B.; Brandes, S.; Tasior, M. *Org. Lett*. **2002**, *4*, 4491.

(6) Tetrapyrranes **9** and **10** were synthesized from acid-catalyzed condensation of corresponding dipyrromethane dicarbinol with pyrrole.

(7) Shin, J.-Y.; Furuta, H.; Osuka, A. *Angew. Chem., Int. Ed*. **2001**, *40*, 619.

The solution structure was arrived at by a detailed ^{1}H and 2D NMR spectrum of **11** and **13**. As a representative example, the ^{1}H−^{1}H COSY spectrum of **11** along with the correlations observed in the deshielded region (5−8.75 ppm) is shown in Figure 3. The three D_2O-exchangeable signals

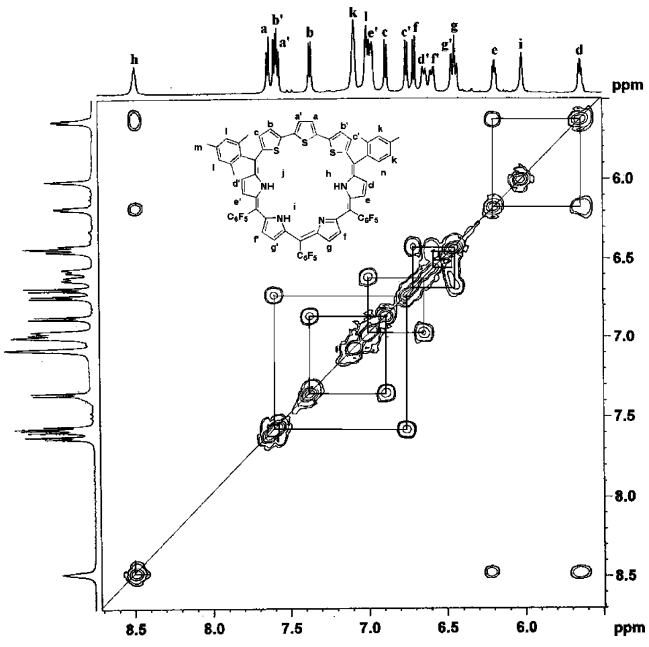


Figure 3. ^{1}H−^{1}H COSY spectrum of **11** in CD_2Cl_2 with assignments observed.

at δ = 11.7, 8.5, and 6.01 ppm were assigned to three NH protons. Seven heterocyclic β-CH's resonate as seven doublets in the region of 5.6−7.6 ppm. On the basis of the above ^{1}H NMR spectral data, **11** was identified as a 32π nonaromatic macrocycle.

In contrast, the ^{1}H NMR of **13** in CD_2Cl_2 revealed its aromatic character. Six doublets in the region of 8.48−9.51 ppm were assigned to six magnetically distinct β-CH in three thiophene rings. The β-CH protons of the two inverted pyrrole rings experience a considerable ring current and are shifted upfield in the region of 2.43−3.84 ppm as four doublets. The remaining four β-CH protons of the two pyrrole rings appeared as four doublets between 7.5 and 7.76 ppm. A broad singlet at 9.38 ppm was assigned to the NH proton of the inverted pyrrole ring. The signal at 7.25 ppm corresponds to the phenyl protons of the *meso*-mesityl rings, and four signals between 2.1 and 2.6 ppm were assigned for the methyl protons of the *meso*-mesityl rings (see Supporting Information). These spectral data suggest that **13** is a 30π aromatic macrocycle.

(8) Upon reduction of **15** and **16** using $NaBH_4$, the color turns from blue to red. However, the reduced forms cannot be isolated as they revert back to the oxidized form during purification.

(9) The presence of disordered TFA in the crystal precludes unambiguous determination of the degree of protonation.

(10) Crystal structure of compound **13** has been deposited at the Cambridge Crystallographic Data Centre with reference no. CCDC 648657.

(11) Shin, J.-Y.; Furuta, H.; Yoza, K.; Igarashi, S.; Osuka, A. *J. Am. Chem. Soc.* **2001**, *123*, 7190.

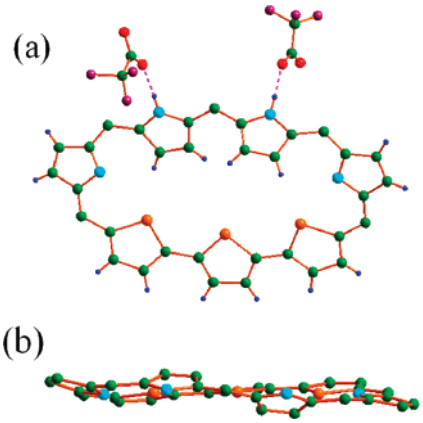


Figure 4. Single-crystal X-ray structure of TFA-bound heptaphyrin **13**: (a) top view (meso aryl groups are omitted for clarity); (b) side view (meso aryl groups and TFA molecules are omitted for clarity).

The confirmation of the proposed structure of **13** in its protonated form came from the single-crystal X-ray structure shown in Figure 4.[9,10] As expected, the two pyrrole rings are inverted, where the imino and amino nitrogens of the pyrrole rings are pointing away from the macrocyclic ring current. Two TFA molecules were bound outside the cavity of the macrocycle, one with imino pyrrolic nitrogen and the other with amino pyrrolic nitrogen in anionic form. Strong N−H···O hydrogen bonding interactions were observed [N3−H3···O6, 1.638 Å, 176.64°] and [N2−H2···O1, 1.796 Å, 174.89°] between inverted pyrrolic nitrogen and carboxylic acid oxygen of the TFA molecule. Overall, the structure is near planar, except for the two inverted pyrrole rings slightly tilted above and below of the macrocyclic mean plane. A similar binding mode of TFA to nitrogen of the inverted pyrrole ring was observed by Osuka and co-workers, leading to a large "cleft"-like conformation.[11]

In conclusion, we have described the syntheses of aromatic 30π heptaphyrin and nonaromatic 32π heptaphyrin with five meso links. These can be interconverted between the oxidized (30π) and reduced (32π) forms by use of simple oxidizing and reducing agents. The synthetic methodology is simple and effective due to the absence of side products and easier purification. Efforts are currently underway to explore the binding of guest molecules inside the macrocycle as well as their coordination chemistry.

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Supporting Information Available: Experimental procedures and characterization of all new compounds, UV−vis spectra of TFA titration for **11** and **13**, and crystallographic data for compound **13** in CIF format, This material is available free of charge via the Internet at http://pubs.acs.org.

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