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Core-Modified Hexaphyrins; Characterization of Two- and Four-Ring Inverted 26 π Aromatic Macrocycles

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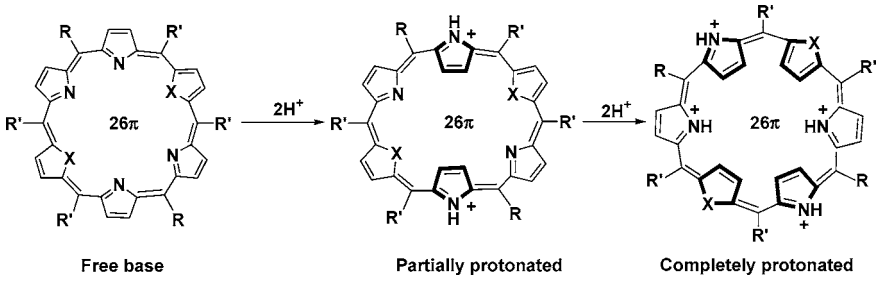
ABSTRACT



Synthesis and structural characterization of aromatic core-modified 26 π hexaphyrin analogues are reported.

Hexaphyrins are a class of expanded porphyrins with six pyrrole rings interconnected to each other through six meso carbon atoms.[1] The presence of six meso carbon bridges makes the molecule flexible, and hence hexaphyrins generally adopt different conformations. The substituents present on the β-pyrrole and meso aryl groups influence the conformation. Even though the synthesis of hexaphyrin[2] **1** was reported in 1983, the advances in its chemistry are more recent. Cavaleiro and co-workers[3] were the first to characterize by X-ray diffraction analysis the structure of hexaphyrin **2**, which shows a partially inverted structure with two opposite pyrrole rings undergoing 180° ring flipping. Dolphin and co-workers[4] reported the synthesis of **3**, which turned out to be unstable and hence not amenable to structural characterization. More recently, hexaphyrins bearing both β-pyrrole and meso substituents **5** and **6** were reported by Anderson,[5] Osuka, and Furuta.[6] Both **5** and **6** are figure-eight-shaped with no ring inversion. The synthesis of **4** is known without any characterization and structural details.[7]

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(5) Krivakapic, A.; Cowley, A. R.; Anderson, H. L. *J. Org. Chem.* **2003**, *68*, 1089−1096.

(6) (a) Shin, J.-Y.; Furuta, H.; Yoza, K.; Igarashi, S.; Osuka, A. *J. Am. Chem. Soc.* **2001**, *123*, 7190−7191. (b) Shimizu, S.; Shin, J.-Y.; Furuta, H.; Ismael, R.; Osuka, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 78−82. (c) Taniguchi, R.; Shimizu, S.; Suzuki, M.; Shin, J.-Y.; Furuta, H.; Osuka, A. *Tetrahedron Lett.* **2003**, *44*, 2505−2507.

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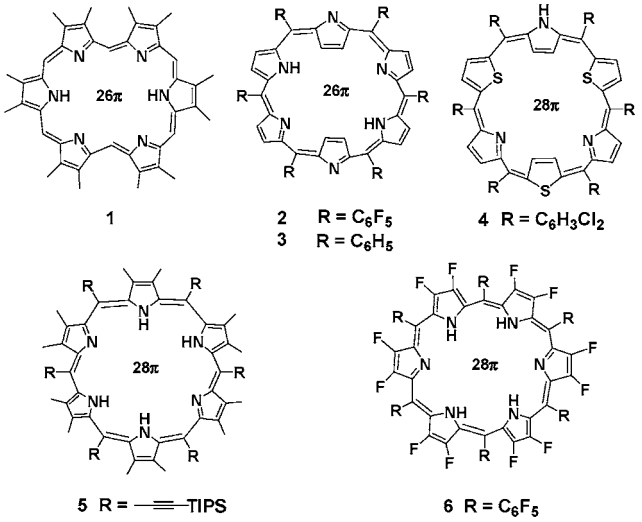
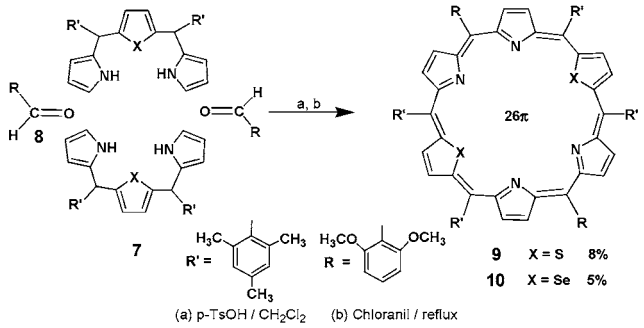


Of the six hexaphyrins known to date, only **1** and **2** exhibit aromatic character, while **4**−**6** are nonaromatic 28 π macrocycles. Thus, the synthesis of hexaphyrins bearing different substituents is important not only for the development of methodology but also to understand their structural diversity and aromatic character. In this communication, we wish to report the synthesis and structural characterization of hexaphyrin analogues bearing two different meso substituents [Scheme 1]. It has been shown that **9** and **10** exhibit dynamic structural behavior in the free-base form, while in the partially protonated state, the single-crystal X-ray structure indicates inversion of two opposite pyrrole rings. In the completely protonated state, variable-temperature ^{1}H and two-dimensional NMR studies reveal 180° ring flipping of two additional heterocyclic rings leading to four-ring inverted macrocycles.

Scheme 1



The synthesis involves MacDonald-type acid-catalyzed condensation of modified tripyrrane[8] **7** with 2, 6-dimethoxy benzaldehyde **8** in methylene chloride followed by chloranil oxidation under reflux. The yield of hexaphyrin was dependent on the concentration of the acid catalyst.[9] Maximum yields are obtained with 0.5 equiv of *p*-toluenesulfonic acid. Increasing the acid concentration to 1 and 2 equiv reduces the yield to less than 1%. Doubling the aldehyde concentration does not have any effect on the yield. Despite the low yields, the advantage of the methodology is the isolation of single product leading to easy purification by column chromatography. It should be mentioned here that all the previous syntheses of hexaphyrins reported in the literature give mixtures of products where the separation of pure forms was not easy. The mechanism of formation of **9** and **10** is based on the well-known MacDonald synthesis of porphyrins.[10]

The proposed structure for various forms of **9** and **10** were confirmed by different spectroscopic techniques and the single crystal X-ray structure of partially protonated form of **9**. The FAB mass spectra show a M^+ peak at *m*/*z* 1243 for **9** and *m*/*z* 1337 for **10**, confirming the composition for free-base form. The completely protonated form of **9** and **10** exhibit well-resolved peaks in ^{1}H NMR at 228 K for **9** and 238 K for **10**, and we were successful in complete assignment of all the peaks [Figure 1]. Specifically for **9**,

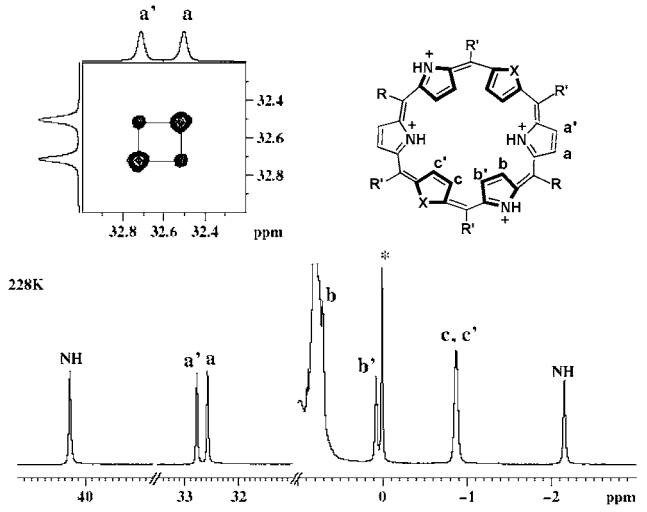


Figure 1. ^{1}H NMR spectrum of completely protonated **9** in $CDCl_3$ at 228 K in selected regions. Assignments are marked. The correlation observed for a and a′ protons in two-dimensional COSY is shown in the inset.

the β-CH protons of inverted pyrrole rings (b,b′) appear at 0.68 and 0.08 ppm, while the β-CH protons of the inverted thiophene rings (c,c′) appear at −0.88 ppm. The inner NH

(8) Narayanan, S. J.; Sridevi, B.; Chandrashekar, T. K.; Vij, A.; Roy, R. *J. Am. Chem. Soc.* **1999**, *121*, 9053−9068.

(9) In a typical procedure, modified tripyrrane **7** (0.6 g, 1.25 mmol) was reacted with **8** (0.2 g, 1.25 mmol) in dry dichloromethane (250 mL) and stirred under a nitrogen atmosphere in the absence of light for 15 min. *p*-Tolyl sulphonic acid (0.11 g, 0.62 mmol) was added and stirring continued for 90 min. The reaction mixture was exposed to air, and chloranil (0.3 g, 1.25 mmol) was added; the reaction mixture was refluxed for 90 min on a preheated oil bath. The solvent was removed under reduced pressure. Upon purification by column chromatography with alumina (basic, grade III), a pink band eluted with 2:3 dichloromethane/petroleum ether, which on solvent evaporation afforded **9** as a dark green solid [120 mg, 8%].

(10) Smith, K. M. In *Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol.1, pp 1−44.

protons of the noninverted pyrrole rings appear as a sharp singlet at −2.16 ppm. The NH proton of the inverted pyrrole ring appears as a sharp singlet at 40.22 ppm, further confirming the pyrrole ring inversion. The β-CH protons of the noninverted pyrrole rings (a,a′) appear at 32.58 and 32.77 ppm, which show correlation between themselves. Furthermore, the ^{77}Se NMR of the completely protonated form of **10** shows a single peak at approximately 495 ppm, confirming the inversion of selenophene rings (see Supporting Information for details). Thus, the NMR spectrum clearly reveals the presence of twofold symmetry in the completely protonated state. The aromatic nature of the protonated forms of **9** and **10** is evident from the large $\Delta\delta$ values [42.38 for **9** and 31.22 ppm for **10**] observed. The electronic absorption spectra in Figure 2 show intense Soret-type and weak Q-type

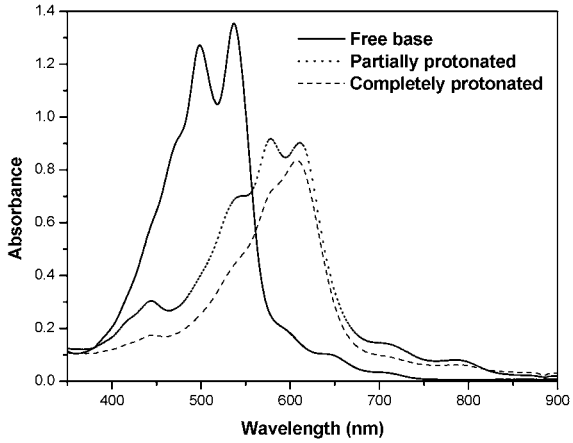


Figure 2. Electronic absorption spectra of **9** [$\sim 10^{-6}$ M] and the protonated derivative in CH_2Cl_2. Protonation is achieved by the careful addition of dilute solution of TFA in CH_2Cl_2.

bands in the visible region, confirming the porphyrinoid nature of the macrocycle. The observation of split Soret bands both in the free-base and protonated forms indicate a nonplanar conformation. The ϵ values of the Soret absorptions are on the order of 105, further confirming the aromatic nature of the hexaphyrins.[5] The large red shift observed upon complete protonation is typical of meso aryl-expanded porphyrins.[11]

Further confirmation of the proposed structure comes from the single-crystal X-ray structure of the partially protonated form of **9**. The structure depicted in Figure 3 shows that the opposite pyrrole rings, which are protonated, are inverted

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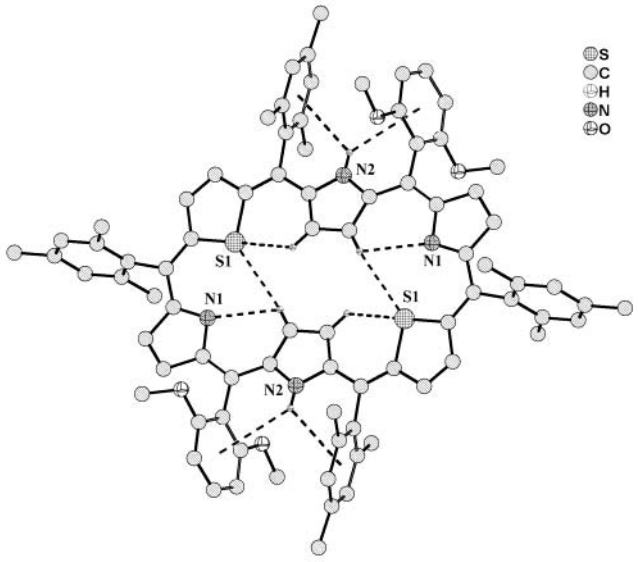

Figure 3. Crystal structure of partially protonated **9** (top view). Hydrogen bonded interactions are shown with dotted lines.

and above and below the plane of the macrocycle defined by the six meso carbons by 17.14°. There are two C−H- - -N interactions [2.536 Å, 110.94°] and two kinds of C−H- - -S interactions [2.686 Å, 114.26°; 2.803 Å, 150.76°] within the cavity of the macrocycle. Furthermore, the inverted pyrrole NH protons are involved in N−H- - -π interactions [2.905 Å, 128.96°; 2.955 Å, 128.95°] with the adjacent meso aryl rings.

In summary, we have successfully described the syntheses and characterization of modified hexaphyrins containing thiophene and selenophene rings via a (3 + 3) acid-catalyzed MacDonald-type condensation reaction. It has been shown that the conformation of these hexaphyrins is critically dependent on the nature of meso substituents and the state of protonation. Further studies are in progress to explore their rich structural diversity.

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Supporting Information Available: Characterization data, including FAB mass, UV−vis data, ^{1}H NMR, and two-dimensional NMR, and CIF file of **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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