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Meso Aryl Heptaphyrins: The First 30π Aromatic Expanded Porphyrins with an Inverted Structure

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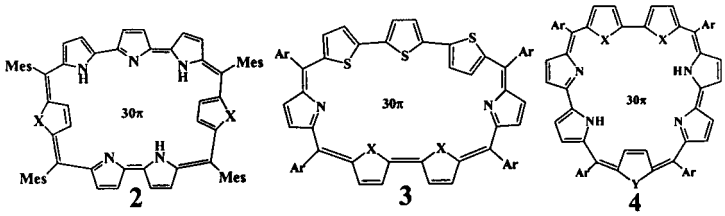
ABSTRACT



Synthesis of new meso aryl 30π heptaphyrins 2, 3, and 4 is achieved. Spectroscopic studies reveal that 2, 3, and 4 are aromatic and possess an inverted structure.

The unique physical and chemical properties and diverse biomedical applications displayed by cyclic polypyrroles have stimulated a large amount of research in the area of expanded porphyrins.[1] A variety of expanded porphyrins containing up to six pyrrole/heterocyclic rings have been synthesized, and their properties such as receptors for anions, ligands for metals, sensitizers for PDT, and as MRI contrasting agents have been exploited recently.[2,3] However, only a few expanded porphyrins containing more than six pyrrole rings are reported to date. They are the 8 pyrrolic octaphyrins,[4] the 10 pyrrolic turcasarin,[5] the 12 pyrrolic dodecaphyrin, and the 16 pyrrolic hexadecaphyrin.[6] These macrocycles are not only interesting from the structural point of view since they exhibit various nonplanar or figure eight conformations but also for their applications in anion binding and as catalysts in enantioselective reactions.[7] However, all these macrocycles turned out to be nonaromatic.

Surprisingly, the expanded porphyrins containing seven and nine pyrrole rings have hitherto escaped all efforts at their synthesis. Very recently Sessler and co-workers[4d] were successful in the synthesis of the nonaromatic 28π heptaphyrin [1.0.0.1.0.0.0] **1** by an acid-catalyzed condensation of tetrapyrrole dialdehyde with bipyrrole, which afforded an open chain heptapyrrole that upon subsequent cyclization

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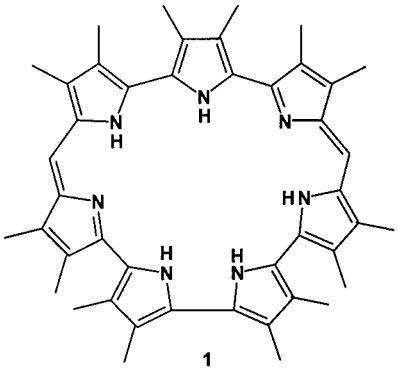
afforded **1**. Inspite of this success, the need to synthesize other new systems for an understanding of aromaticity, π



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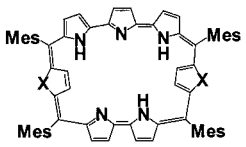
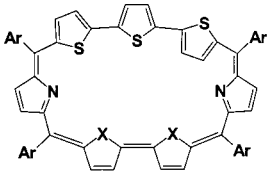
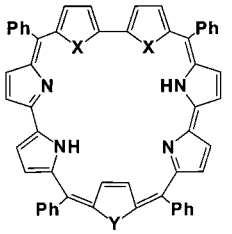
conjugation, and the effect of heteroatom substitution still remains, and in this Letter, we wish to report the successful syntheses of three different kinds of heteroatom-containing meso aryl heptaphyrins, **2**, **3**, and **4**, by an easy and efficient synthetic methodology. Unlike **1**, the heptaphyrins **2**, **3**, and **4** are *aromatic* and exhibit inverted structures where one or two heterocyclic rings have undergone a 180° ring flipping.



X = S 2a
X = Se 2b



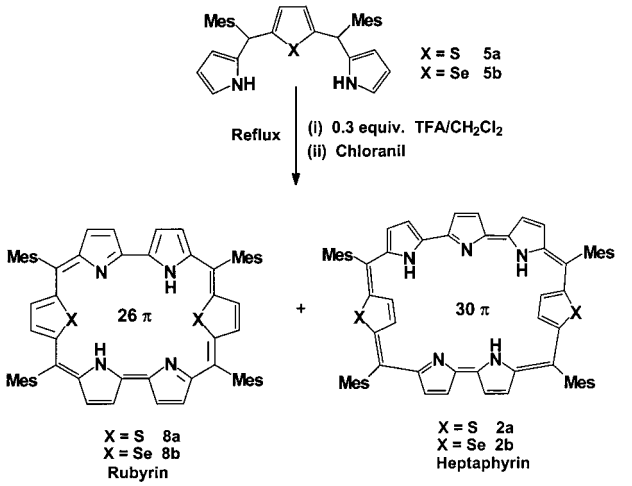
	Ar	X
3a	Mes	S
3b	Ph	S
3c	Ph	O
3d	Ph	Se



	X	Y
4a	S	S
4b	S	Se
4c	Se	S
4d	Se	Se

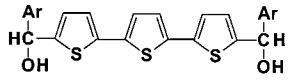
The first clue that the meso aryl heptaphyrins could be synthesized came from the reaction of mesityl tripyrranes **5a** or **5b** containing heteroatoms in the presence of 0.3 equiv of TFA as catalyst in dichloromethane, followed by chloranil oxidation (Scheme 1). After a basic workup and chromatographic purification, two major products were isolated. They are 26π rubyrins **8a** or **8b** in 15% yield and 30π heptaphyrins **2a** or **2b** in about 2% yield. The formation of trace amounts of 18π porphyrin and 22π sapphyrin were also noticed. We have recently shown that modified tripyrranes are not very stable under the reaction conditions and undergo acid-catalyzed fragmentation.[8] The fragmented products recyclize to give a mixture of porphyrins and expanded porphyrins. The tripyrranes bearing the meso phenyl groups gave only

Scheme 1

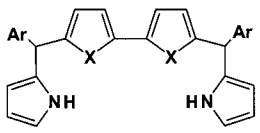


porphyrins, sapphyrins and rubyrins, while the tripyrranes bearing the meso mesityl groups gave an additional product, which was 30π heptaphyrin. This is probably due to the increased steric bulk on the meso phenyl ring, which is in accord with the observation of Setsune and co-workers[6] in the Rothemund reaction of bipyrroles with 2,6-dichlorobenzaldehyde. The formation of the heptaphyrin can be rationalized by considering the fragmentation of tripyrranes and the recombination of the fragmented product.[9]

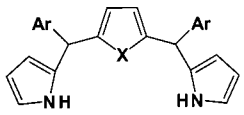
To synthesize meso aryl heptaphyrins in good yield, a more rational synthesis was designed with easily available precursors, either through a [4 + 3] MacDonald type condensation or through an oxidative coupling reaction. The key precursors required were hitherto unknown: 5,5″-bis-(arylhydroxymethyl)-2,2′:5,2′-terthiophene **6** and 5,14-diphenyl-20,21-diselenatetrapyrromethane **7d**. **6** was synthesized by a reaction of terthiophene with *n*-butyllithium followed by treatment with aryl/mesityl aldehyde in 75% yield. **7d** was



Ar = Ph 6a
Ar = Mes 6b



	Ar	X
7a	Mes	S
7b	Ph	S
7c	Ph	O
7d	Ph	Se



	X	Ar
5a	S	Mes
5b	Se	Me
5c	S	Ph
5d	S	Ph

synthesized in 85% yield by a reaction of biselenophene diol and pyrrole with TFA as the catalyst, using a method similar to the one reported by us for the synthesis of **7b**.[10] Thus, reaction of **6a** with **7b**, **7c**, or **7d** with 1 equiv of TFA in dichloromethane, followed by oxidation with chloranil gave **3b**, **3c**,

or **3d** as the only product (yield for **3b** is 22%, for **3c** is 20%, and for **3d** is 15%). **3a** was synthesized by reacting **6b** and **7a** in 20% yield. **3a**−**3d** display a deep purple color in organic solvents. On protonation with acid, the color changes immediately to indigo. The heptaphyrins **4a**−**4d** were synthesized in 15−20% yield through oxidative coupling reactions of **5c** or **5d** with **7b** or **7d** in dichloromethane containing 2 equiv of TFA, where the two pyrrole−pyrrole links were formed at the final step through α−α coupling.[8d]

The compositions of the heptaphyrins **2**, **3**, and **4** were established from the FAB mass spectra and the analytical data. The solution structure was arrived at by a detailed analysis of proton NMR spectra. For the complete assignment of all the peaks, 2D H,H-Cosy was required. As a representative example, the ^{1}H NMR spectra of **3a** along with the correlations observed in H,H-Cosy in the aromatic region and in the shielded region are shown in Figure 1. There are

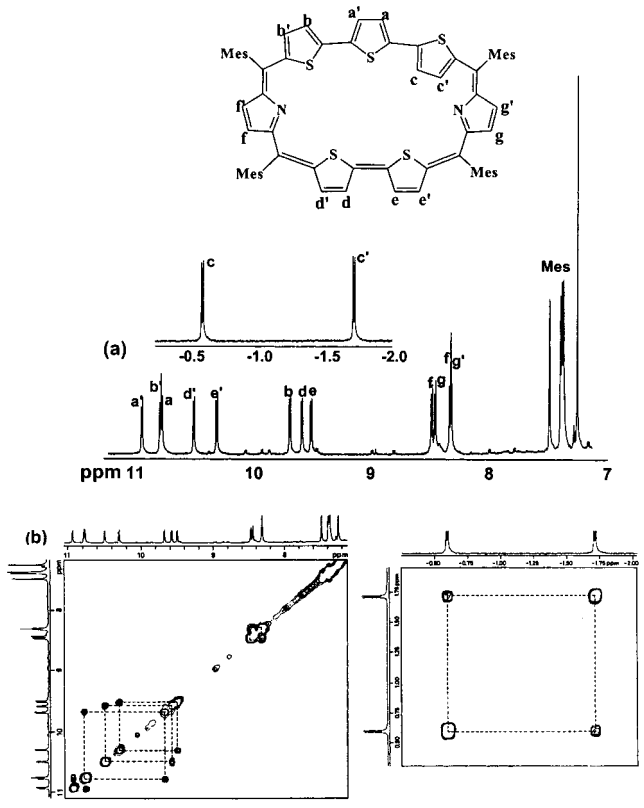


Figure 1. ^{1}H NMR spectrum of **3a** in $CDCl_3$: (a) in the aromatic region. The inset shows the high-field region. (b) 2D H,H-Cosy in the aromatic and the shielded region. The correlations are shown by dotted lines.

10 β-CH protons on the thiophene rings. Eight of them (aa′, bb′, dd′, and ee′) resonate in the aromatic region between 9.2 and 10.2 ppm, and the remaining two protons (cc′) appear as two doublets in the shielded region between −0.5 to −1.5 ppm. The pyrrole protons (ff′ and gg′) also appear as individual doublets in the region 8.5 to 8.2 ppm. These assignments were made on the basis of the correlation seen in the H,H-Cosy (Figure 1b). The appearance of individual doublets for each proton reflects the lower symmetry of the molecule, and the observation of two doublets in the high-field region suggested that one of the thiophene rings is inverted and protons of the inverted ring are experiencing the ring current of the macrocycle. One can envisage two possibilities as to which of the thiophene rings is inverted. They are (a) the central thiophene ring of the terthiophene unit or (b) one of the terminal thiophenes of the terthiophene unit or the thiophene ring of the bithiophene unit containing the ee′ protons. The inversion of the central thiophene ring containing the aa′ protons is ruled out on the basis of the symmetry considerations. Such a ring inversion leads to the presence of a symmetry axis passing through the central S atom and center of the opposite bithiophene rings containing the dd′ and ee′ protons, which would result in fewer peaks in the NMR spectrum than observed. This leads to the possibility where either of the thiophene rings containing the cc′ or bb′ protons is inverted and such a ring inversion would lead to lowering of the symmetry of the molecule leading to the inequivalence of all the thiophene protons as observed. The possibility of inversion of thiophene ring containing ee′ protons is ruled out on the basis of our previous work on rubyrin and the structure of modified tripyrromethanes, where the ring inversion was observed in the tripyrromethane moiety itself.[8b] Such a ring inversion has been observed earlier by others[11] and us for the sapphyrins and modified rubyrins containing meso aryl substituents.[8]

The chemical shifts of the inverted thiophene ring protons were found to be dependent on temperature, and at lower temperatures these protons are shifted further upfield. A variable temperature spectral study for these protons for **3d** suggests that the inverted thiophene ring is experiencing a slow rotation on the NMR time scale, and the further shielding observed for these protons at lower temperature suggests that these protons are exposed to the ring current of the macrocycle. The protonation of the pyrrole nitrogens by a careful titration of TFA leads to a downfield shift of pyrrole, thiophene, and bithiophene protons, while the protons of the inverted ring shift further upfield. For example, for diprotonated **3d**, the inverted ring protons resonate between −3 to −4 ppm (relative to +0.6 to −0.75 ppm for the free base) and the NH protons resonate as two individual singlets in the region −4 to −5 ppm. This observation suggests that upon protonation the inverted ring becomes more planar and feels the effect of the ring current of the macrocycle. The Δd values (the chemical shift difference

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between the inner and the outer protons) for the protonated derivatives vary in the range 13−17 ppm (for example, for **3b**, 16.6 ppm; **3c**, 15.9 ppm; **3d**, 15.8 ppm), clearly suggesting the aromatic nature of the heptaphyrins and also accounting for the presence of 30π electrons according to the $4n + 2$ rule. *To the best of our knowledge these are the first examples of meso aryl expanded porphyrins containing seven heterocyclic rings having an inverted structure and displaying aromaticity.*

Further proof of the aromaticity comes from the electronic absorption spectral studies. The spectra for free base and protonated forms of **3b** shown in Figure 2 indicates the

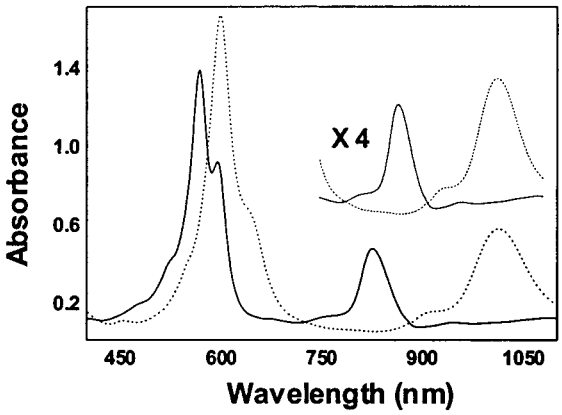

Figure 2. Electronic absorption spectra of 4.46×10^{-6} M **3b** (—) and its dication (·····) in dichloromethane.

presence of intense Soret type bands in the region 560−570 nm and four Q-bands in the region of 750−1100 nm. A comparison of these values with the corresponding rubyrins shows red shift of absorption bands, in agreement with the extended conjugation.[8b] These absorption bands are also red shifted relative to **1**, reflecting the effect of heteroatom substitution. The ϵ value of the free base form is about six times higher than that observed for **1**. Protonation by addition of a dilute solution of TFA in dichloromethane leads to further red shifting of the Soret and Q-bands; this effect is typical of meso tetra aryl porphyrins.[8] Additional evidence for the aromatic character comes from the preliminary cyclic voltametric studies. **3b** and **3d** exhibit two reversible reductions and two irreversible oxidations. A comparison of these data with corresponding tetra aryl porphyrin suggests the stabilization of LUMO's of **3b** and **3d** by 440 and 470 mV, respectively. An estimated HOMO−LUMO gap of 1.29V for **3b** and 1.38V for **3d** indicates a significant reduction relative to meso aryl rubyrin and sapphyrin (for sapphyrin it is −1.88 V and for rubyrin it is −1.64 V), thus explaining large red shifts observed in the electronic spectrum.[8a]

In conclusion, we have successfully synthesized the first examples of aromatic meso aryl 30π heptaphyrins which exhibit three different types of inverted structures.

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Supporting Information Available: Tables of UV−vis absorption data, ^{1}H NMR spectra, CV, mass spectra, and temperature-dependent ^{1}H NMR spectra in freebase and protonated forms for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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