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Letter

# Symmetric $32\pi$ (1.0.1.0.1.0.1) Core-Modified Heptaphyrins from Asymmetric Building Block

Prachi Gupta and Venkataramanarao G. Anand\*



**ABSTRACT:** An asymmetrical precursor with three thiophene subunits on condensation with a thiophene/furan diol yield a symmetrical  $32\pi$  heptaphyrin. Here are the first examples of pyrrole-free antiaromatic heptaphyrin synthesized by the acid assisted condensation reaction, followed by an oxidative  $\alpha - \alpha$  coupling between the terminal thiophene rings. The macrocycles attains a slightly bent configuration, which undergoes reversible two-electron oxidation between a neutral  $4n\pi$  and  $(4n + 2)\pi$  dication state.

H eptaphyrins are a class of porphyrnoids with seven heterocycles in the core of the macrocycle. These heterocyclic units are covalently linked together with a varying number of bridging carbons within a given macrocycle. A macrocycle with seven pyrrole units and two bridging carbons (Figure 1) was the first heptaphyrin, 1, to be synthesized via [3 + 2 + 2] oxidative coupling of oligo pyrroles under acidic conditions.<sup>1</sup> It was identified as a  $28\pi$  nonaromatic macrocycle with a planar geometry. A nonplanar  $30\pi$  heptaphyrin with all



Figure 1. Pyrrole containing heptaphyrins with different *meso* positions.

pyrrole rings and five meso positions was also reported by the same group.<sup>2</sup> Few other heptaphyrins bearing four to seven bridging carbons were synthesized by replacing a few pyrrole units with other heterocycles, such as furan/thiophene/ selenophene. Aromatic  $30\pi$  heptaphyrins were synthesized via [4 + 3] acid-catalyzed condensation reaction, followed by oxidation.<sup>3,4</sup> Pyrrole's innate ability to undergo reversible amine-imine inter conversion aids global  $\pi$  conjugation in these heptaphyrins. Accordingly, heptaphyrins  $[2 \text{ and } 3]^5$  with five meso positions and four pyrrole rings were known to attain  $32\pi$  and  $30\pi$  structures, respectively. Furthermore, they were redox inter convertible between aromatic and antiaromatic states in the presence of suitable oxidizing and reducing agent, respectively. Another  $32\pi$  pyrrolic heptaphyrin, 4, with seven meso positions was found to adopt a twisted configuration to display Mobius aromatic behavior.<sup>6</sup>

Except for the above-mentioned few examples, heptaphyrins are relatively unfamiliar, in comparison to their immediate macrocyclic cousins, hexaphyrin<sup>7</sup> and octaphyrin.<sup>8</sup> This can be partially attributed to the comparatively asymmetrical nature of the seven membered macrocycle. Furthermore, nonpyrrolic heptaphyrins are not known to the best of our knowledge. Recent studies have revealed that replacing all the pyrroles by

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thiophene/furan in a porphyrin leads to the antiaromatic isophlorin-like macrocycle.<sup>9</sup> In contrast to the parent aromatic porphyrin, antiaromatic porphyrinoids are susceptible to reversible two-electron oxidation and, hence, provides a redox switch between  $4n\pi$  and  $(4n + 2)\pi$  states of a given macrocycle.<sup>10</sup> By considering the challenges associated with the synthesis of heptaphyrins, we envisaged to explore the synthesis, electronic, and redox properties of novel nonpyrrolic heptaphyrins.

Herein, we employed thiophene subunits in the synthesis of heptaphyrins. Invariably, symmetrical precursors have been employed for the synthesis of expanded porphyrinoids.<sup>11</sup> In a modified approach, we designed a novel asymmetric trithiophene precursor, 7, consisting of bithiophene and thiophene subunits. A synthetic protocol was developed by condensing thiophene mono alcohol  $5^{13}$  with excess of 2-bromothiophene using amberlyst-15 as a catalyst in darkness and under inert conditions to obtain 6 in 90% yields. It was further subjected to Kumada coupling<sup>12</sup> with 2-bromothiophene for 40 h to produce 7 in 35% yield (see Scheme 1). Two

Scheme 1. Synthesis of Novel Asymmetric Trithiophene



equivalents (2 equiv) of trithiophene 7 were condensed with 1 equiv of thiophene diol, 8a,<sup>14</sup> in dichloromethane by adding 1 equiv of BF<sub>3</sub>·OEt<sub>2</sub> in darkness and under inert conditions (see Scheme 2).

Subsequent oxidation with DDQ led to the ring closing  $\alpha - \alpha$  coupling of terminal thiophenes to yield the heptaphyrin, 9. The formation of macrocyclic hepta thiophene was confirmed by Matrix Assisted Laser Desorption Ionization - Time Of

Scheme 2. Plausible Heptaphyrins from a 2:1 Condensation



Flight/Time Of Flight (MALDI-TOF/TOF) mass spectrometry. Depending on the oligomerization of transient species prior to oxidative ring closing, head-to-head (H-H), **9a**, or head-to-tail (H-T), **9b** or tail-to-tail (T-T) **9c** for the same m/zare feasible in this synthetic protocol. Despite the altered connectivity, all three structures adhere to a formal count of 32  $\pi$ -electrons along their respective conjugated pathway. However, from chromatographic separation, only one heptaphyrin could be identified and isolated in 11% yields as a brown-colored band from the reaction mixture. We observed a similar result upon replacing thiophene diol by furan diol, **8b**, under identical reaction conditions.

The isolated brown colored solution displayed an absorption maximum at 500 nm ( $\varepsilon = 262\ 000\ \text{L}\ \text{mol}^{-1}\ \text{cm}^{-1}$ ), along with a shoulder-like band at 468 nm (133 000) (Figure 2A). This



Figure 2. Electronic absorption spectra of (A)  $10^{-5}$  M solution of 9a and  $9a^{2+} \cdot 2[SbCl_6]^-$  and (B)  $10^{-5}$  M solution of 10a and  $10a^{2+} \cdot 2[SbCl_6]^-$  in dry dichloromethane. (C, D) Cyclic voltammograms of 9a (panel (C)) and 10a (panel (D)) recorded in dichloromethane at a scan rate of 100 mV s<sup>-1</sup> with 0.1 M tetrabutylammonium perchlorate as the supporting electrolyte.

spectrum resembled the characteristics of a typical expanded porphyrinoid while negating an admixture of structural isomers in the solution. <sup>1</sup>H NMR spectroscopy of the isolated species further buttressed the exclusive formation of a discrete  $32\pi$ macrocycle. At room temperature, it displayed a well-resolved <sup>1</sup>H NMR spectrum consisting of six doublets and a singlet in the region between  $\delta$  5.0 to 6.0 ppm. All the resonances corresponded to an equal number of protons. In stark contrast to many expanded porphyrnoids,<sup>11</sup> lack of fluxional behavior was emphasized by a well-resolved spectrum at room temperature. Observation of relatively upfield shifted resonances for the  $\beta$ -protons of thiophene in comparison to 7 justified the moderate paratropic ring current effect for the antiaromatic  $32\pi$  macrocycle. Moreover, it also implied that none of the thiophene units adopted a ring inverted conformation in the macrocycle (see Figure S13 in the Supporting Information). <sup>1</sup>H-<sup>1</sup>H COSY spectrum confirmed the three sets of doublets coupled to each other (see Figure S14 in the Supporting Information). The six doublets can be attributed to the  $\beta$ -protons of the asymmetrical thiophene unit, 7 and the solitary singlet can be attributed to  $\beta$ -protons of the thiophene diol, 8a. Since this spectrum represented a

macrocycle with a  $C_2$  axis of symmetry, it could be concluded that the isolated molecule does not represent the plausible asymmetrical structure of heptaphyrin **9b**. Quantum computational calculations further revealed that **9b** was higher in energy than **9a** or **9c**, by more than 14 kcal/mol (see Table S1 in the Supporting Information). Yet, NMR spectroscopy could not distinguish the  $C_2$  axis of symmetry between **9a** and **9c**.

Finally, the molecular structure was unambiguously established from single-crystal X-ray diffraction (XRD) analysis. Consistent with the <sup>1</sup>H NMR spectrum, it revealed a slightly bent geometry and confirmed the structure of macrocycle as **9a** (see Figures 3A and 3B). The S atoms of all



Figure 3. Molecular structure of 9a [(A) top view and (B) lateral view], (C)  $[9a]^{2+}\cdot 2[CF_3SO_3]^-$ , and (D)  $[10a]^{2+}\cdot 2[SbCl_6]^-$  determined from single-crystal XRD studies.

of the thiophene rings were facing the center of the macrocycle, and the phenyl rings were close to orthogonal orientation, with respect to the plane of the molecule defined by the bridging carbon atoms. Furthermore, the estimated Nucleus Independent Chemical Shift (NICS)<sup>15</sup> value of  $\delta$  + 9.90 and the Anisotropy of the Induced Current Density (ACID)<sup>16</sup> plot (see Figure S20 in the Supporting Information) support the antiaromatic characteristic of heptaphyrin, **9a**. The absence of **9c** can be attributed to the steric hindrance arising from the quarterthiophene unit within the macrocyclic framework.

Being a  $4n\pi$  macrocycle, **9a** was easily oxidized by Meerwein salt<sup>17</sup> to its corresponding aromatic  $30\pi$  dicatioinc species,  $9a^{2+}$ . Upon oxidation, the color of its solution dramatically changed from brown to deep blue in dichloromethane. A similar color change was observed upon the addition of triflic acid to a solution of 9a in dichloromethane. In either case, the solution displayed an absorption maxima red-shifted by more than 100 nm (Figure 2A) and a new intense band appeared at 616 nm (417 000), followed by low energy absorption at 988 nm (35 300). Few weaker absoprtions were also observed between 800 and 900 nm. Observation of m/2 signal from HR-MS (see Figure S21 in the Supporting Information) further supported the two-electron oxidation of 9a. Upon addition of a base, such as triethyl amine, the dication,  $9a^{2+}$ , was reduced back to its free base 9a, confirming the reversible two-electron redox process. From cyclic voltammetric studies, we were able to identify the two reversible oxidations at +0.47 and +0.56 V (Figure 2C). In their respective <sup>1</sup>H NMR spectra, the chemical

shift values of the aromatic  $9a^{2+}\cdot 2[SbCl_6]^-$  and  $9a^{2+}\cdot 2[CF_3SO_3]^-$  were almost identical and observed in the lowfield region between  $\delta$  12.0–14.5 ppm (see Figure S22 in the Supporting Information). In contrast to the paratropic shifts in the <sup>1</sup>H NMR spectrum of 9a, the dication  $9a^{2+}$ , being aromatic in nature, revealed a diatropic ring current effect for the resonances of thiophene protons (see Figure S22). The estimated NICS value of  $\delta$  –13.03 ppm and the ACID plot (see Figure S27 in the Supporting Information) unequivocally supported the aromatic feature of the dicationic species. Singlecrystal XRD studies of triflate salt revealed the retention of the same macrocyclic geometry in the oxidized state (Figure 3C). The dicationic macrocycle,  $9a^{2+}\cdot 2[CF_3SO_3]^-$ , was flanked by two triflate counteranions with each macrocycle, confirming the oxidation of the heptaphyrin.

In a parallel reaction, condensation of furan diol, 8b,<sup>18</sup> with 2 equiv of trithiophene, 7, also yielded a brown-colored heptaphyrin solution, 10. It was identified from MALDI-TOF/ TOF mass spectrometry of the reaction mixture, which displayed m/z value of 1273.9043 and further isolated from column chromatography. This brown-colored solution in dichloromethane exhibited a twin absorption maximum (Figure 2C) at 498 nm (88 900) and 440 nm (77 900). In its <sup>1</sup>H NMR spectrum at room temperature, it displayed wellresolved resonances both in the high-field and low-field regions (see Figure S29 in the Supporting Information). Two doublets at  $\delta$  5.68, 5.85 ppm along with a multiplet at 6.22 ppm and a singlet at  $\delta$  5.83 ppm, corresponded to an equal number of protons in the high-field region. Two low-field doublets at  $\delta$ 9.43 and 10.01 ppm also corresponded to the same number of protons as for the individual signals in the high-field region. The presence of both shielded and deshielded signals implied the existence of ring inverted heterocyclic units in the macrocycle. The NMR spectra revealed the paratropic ring current effect observed in the  $32\pi$  antiaromatic macrocyle. Since the same number of signals are noted as for 9a, it can be expected that 10 also adopted a  $C_2$  symmetry geometry. Hence, among the three possible structural isomers (recall Scheme 2), 10a-10c, the unsymmetrical 10b is not in sync with the observed <sup>1</sup>H NMR spectrum. Quantum computational calculations further revealed that 10b was higher in energy than by 10a and 10c, by more than 29 kcal/mol. Unfortunately, all our efforts to crystallize 10 were futile and could not decisively decide the structure between 10a and 10c.

In resemblance to 9a, 10 also exhibited exhibit reversible two-electron oxidation with Meerwein salt. Upon oxidation, its blue-colored solution in dichloromethane exhibit a red-shifted and single intense absorption at 633 nm (414 000), followed by low-energy bands at 874 (22 500), 914 (23 300), and 1041 nm (59 600) (Figure 2B). The addition of a base reduced the formed dication to its free base, as monitored using electronic absorption spectroscopy. The blue-colored solution displayed m/2 peak at 636.9548 in its HRMS (see Figure S36 in the Supporting Information), suggesting the formation of a dication. Cyclic voltammetry (CV) studies (Figure 2D) also supported two reversible one-electron oxidations at +0.53 and +0.61 V, respectively. Further support for the formation of  $30\pi$ dicationic species was obtained from <sup>1</sup>H NMR spectroscopy. Even though the pattern of NMR was retained in the oxidized state, the position of signals in 10 were dramatically inverted for the  $30\pi$  dication,  $10^{2+2}$ [SbCl<sub>6</sub>]<sup>-</sup>. The downfield resonances of  $\delta$  9.43 and 10.01 ppm observed in 10, now resonated at  $\delta$  –4.23 and –5.33 ppm (see Figure S37 in the

Supporting Information). On the other hand, the four signals observed between  $\delta$  5.00 and 6.25 ppm were drastically downfield shifted to the region between  $\delta$  11.00 and 12.00 ppm. An explicit difference of more than  $\delta$  17 ppm between the most shielded and deshielded resonances emphasized the diatropic ring current effects in the  $30\pi$  dicationic macrocycle. An identical pattern of <sup>1</sup>H NMR spectrum clearly suggested that  $32\pi$  macrocycle retained the same geometry, even upon oxidation to the dicationic  $30\pi$  species.

Elucidation of the macrocyclic structure (Figure 3D) by single-crystal XRD analysis confirmed the structure of the dication as  $[10a]^{2+} \cdot 2[SbCl_6]^-$ . In support of the <sup>1</sup>H NMR spectrum observed for 10a and its dication, the two thiophene rings adjacent to the furan were found to be inverted. Hence, the  $\beta$ -CH's of these thiophene rings were exposed to the diatropic ring effects of the  $30\pi$  macrocycle, leading to their strong upfield resonances. In addition, two [SbCl<sub>6</sub>]<sup>-</sup> were also detected as counteranions for the oxidized macrocyclic species. The estimated NICS value of  $\delta$  -12.26 ppm and the ACID plot (see Figure S41 in the Supporting Information) clearly supported the aromatic feature of the dicationic species. Since the freebase is also supposed to retain an identical structure, the estimated NICS value of  $\delta$  +8.21 ppm and the ACID plot (Figure S35 in the Supporting Information) for 10a further justified its antiaromatic state.

In summary, we have synthesized two symmetrical  $32\pi$  heptaphyrins from an asymmetric precursor. Despite the probability for three different structural variants of the macrocycle, the reaction favors only a single structural isomer for the heptaphyrin. This study also suggests the altered reactivity of thiophene subunits in an asymmetrical oligomer, as evidenced by the preferential oxidative coupling of terminal thiophenes over the bithiophene unit. Moreover, heterocycles ring inversion is dependent on the nature of the heteroatoms at the center of the macrocycle. They do exhibit reversible two-electron oxidation without altering the topology. It is envisaged that such asymmetrical thiophene oligomers can be an useful building blocks in the synthesis of many other expanded porphyrinoids with an odd number of heterocycle units.

## ASSOCIATED CONTENT

#### **Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00923.

Details of experimental procedures and spectral data of compounds (PDF)

#### Accession Codes

CCDC 2070921–2070923 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data\_request/cif, or by emailing data\_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

## AUTHOR INFORMATION

## **Corresponding Author**

Venkataramanarao G. Anand – Department of Chemistry, Indian Institute of Science Education and Research (IISER), Pune 411008, Maharashtra, India; © orcid.org/0000-0002-7110-7994; Email: vg.anand@iiserpune.ac.in

#### Author

**Prachi Gupta** – Department of Chemistry, Indian Institute of Science Education and Research (IISER), Pune 411008, Maharashtra, India

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c00923

### Notes

The authors declare no competing financial interest.

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