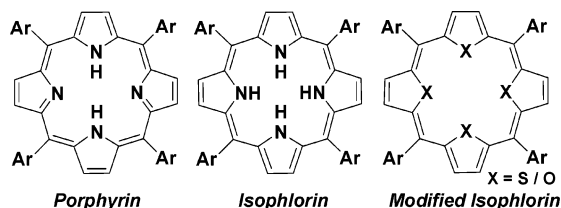


Planar *Meso* Pentafluorophenyl Core Modified IsophlorinsJ. Sreedhar Reddy<sup>‡</sup> and Venkataramanarao G. Anand<sup>\*†</sup>

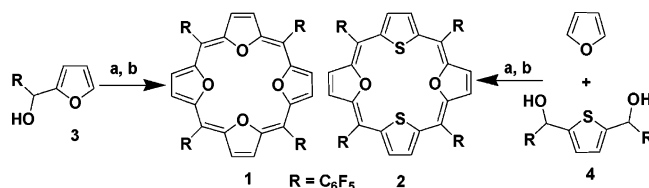
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Isophlorin is a confluence of structural features for annulene and porphyrin. Woodward proposed the tetrapyrrolic  $20\pi$  macrocycle as a hypothetical structure during the synthesis of chlorophyll.<sup>1</sup> Attempts to make isophlorin-like macrocycles have yielded only tetrathia/oxa/selena porphyrin dications<sup>2</sup> (as their perchlorate salts). Vogel and co-workers were successful at characterization of tetraoxaisophlorin in solution state, but X-ray crystallographic analysis was less precise due to static and possible dynamic disorders.<sup>3,4</sup> In contrast to porphyrin, the evolution of isophlorin and its analogues has been hindered by lack of straightforward synthesis and also due to their unstable nature under ambient conditions. So far, isophlorin is not known to be synthesized from simple precursors. It is derived either by reduction of a porphyrin copper complex<sup>5</sup> or by two-electron reduction of *N,N',N'',N'''*-tetramethyloctaethylporphyrin dication.<sup>6</sup> It can rapidly transform itself into an aromatic  $18\pi$  system due to the fast conversion of two of its four cyclic amines to imines. Poor control over this process is an obstacle to explore the chemistry of isophlorins. Replacing nitrogen with divalent oxygen or sulfur in the core and with electron withdrawing substituents on the *meso* carbons can be a plausible way to overcome this drawback. Chalcogens are better alternatives for ring NH, since they can sustain similar structural and electronic features of isophlorins. This conception has been found useful for the facile synthesis of stable isophlorin analogues of thiophene/furan with *meso* pentafluorophenyl substituents. We also wish to report the structural features and impressive supramolecular architectures observed for the first time in isophlorins.



Unlike other aryl aldehydes, pentafluoro benzaldehyde can generate large expanded porphyrins through a one-pot Rothmund-type synthesis.<sup>7</sup> Its reactivity with other heterocycles was unknown until we reported the formation of stable  $30\pi$  and  $40\pi$  macrocycles from furan.<sup>8</sup> Surprisingly, the  $20\pi$  21,22,23,24-tetraoxaisophlorin, **1**, could not be detected in the reaction mixture. The stable higher analogues suggested that the tetraoxa macrocycle can also be engineered with similar *meso* pentafluorophenyl substituents. In an alternative synthetic procedure, 2-pentafluorophenylhydroxymethyl furan **3** was self-condensed by an acid-catalyzed reaction, followed by  $\text{FeCl}_3$  oxidation (Scheme 1). After routine workup and purifica-

Scheme 1. Synthesis of **1** and **2**<sup>a</sup><sup>a</sup> (a) 1 equiv of  $\text{BF}_3 \cdot \text{OEt}_2$ ,  $\text{CH}_2\text{Cl}_2$ , 2 h. (b) 5 equiv of  $\text{FeCl}_3$ , 2 h.

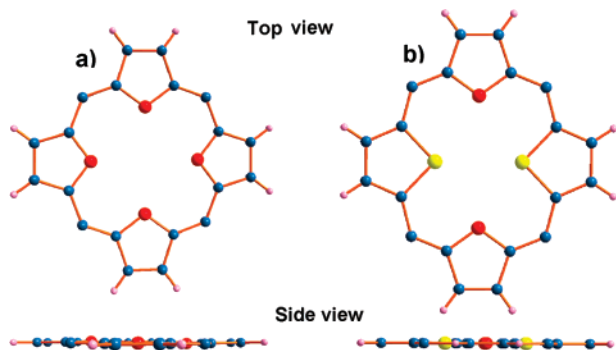
tion by column chromatography, **1** was isolated in 2.5% yields along with other higher congeners<sup>8</sup> ( $30\pi$  and  $40\pi$  macrocycles). Under similar conditions, furan reacts with 2,5-bis(pentafluorophenylhydroxymethyl)thiophene **4** to yield 21,23-dioxa-22,24-dithiasophlorin, **2**, in 6% yields. A larger homologue was also identified in the reaction mixture.<sup>10</sup> Both the macrocycles, **1** and **2**, form green-colored solutions in common organic solvents and yield brown-colored microcrystalline solids upon recrystallization from dichloromethane and hexanes.

These macrocycles show intense absorption in the ultraviolet and visible region of the electromagnetic spectrum (see the Supporting Information). **1** exhibits strong absorption at 320 nm ( $\epsilon = 22\,120$ ) and 357 nm (30 650), while **2** absorbs at 344 nm (31 000) and 376 nm (46 330). They also show four weak absorptions in region 400–500 nm. These absorptions do not change upon addition of oxidizing agents (such as trifluoroacetic acid, DDQ, and iodine). When an excess of perchloric acid (more than 150 equiv) was added, a distinct change was observed in their electronic absorption spectrum (Supporting Information). It resembled an  $18\pi$  porphyrin-type spectrum with a Soret-like absorption at 392 nm and a Q-like band at 710 nm for **1** and at 406, 668, and 708 nm for **2**. This can be attributed to their dicationic species in their oxidized form.<sup>5,6</sup> They were found to be unreactive with reducing agents such as  $\text{LiAlH}_4$  and  $\text{NaBH}_4$ .

Mass spectrometric analysis confirmed the composition of the macrocycles (Supporting Information). Spectroscopic evidence from  $^1\text{H}$  NMR analysis revealed high symmetry for both the macrocycles. The signals observed in the NMR spectrum of both **1** and **2** represent the  $\beta$ -hydrogens of the heterocyclic rings (Supporting Information). A sharp singlet at  $\delta$  2.49 ppm was observed for tetraoxa isophlorin **1** indicative of identical furans in the macrocycle. The protons of thiophene and furan in **2** resonate as two sharp singlets at 3.37 and 3.33 ppm, respectively. The significant upfield chemical shifts are attributed to the considerable paratropic ring current effects, and to the best of our knowledge these are the highest ever to be recorded for stable isophlorin systems. Therefore both the macrocycles are expected to adopt planar conformation.

So far, only nonplanar conformations and structure-induced loss of paratropicity are observed in isophlorins.<sup>5,6</sup> Conversely, single-crystal X-ray diffraction studies (Figure 1) of **1** and **2** confirmed the planar conformation in support of  $^1\text{H}$  NMR analysis. Both the

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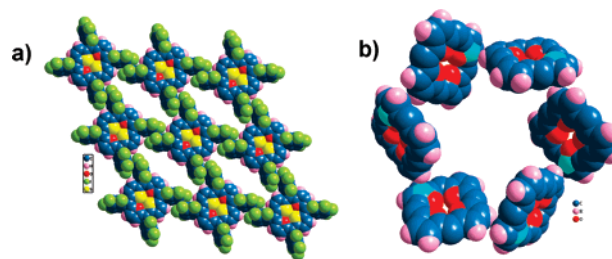


**Figure 1.** Single-crystal X-ray structure of **1** (a) and **2** (b): O (red), C (blue), S (yellow), and H (pink). *meso*-Pentafluorophenyl rings and the solvent molecules are omitted for clarity.

macrocycles show remarkable planarity for the  $20\pi$  isophlorin system. All the heterocyclic rings, in both the macrocycles, are in the same plane as that of the *meso* carbons, while the pentafluorophenyl substituents are perpendicular to the plane of the macrocycle. In **1** (Figure 1a), the interatomic distance between diagonal oxygen atoms was found to be  $4.13 \text{ \AA}$ , whereas in **2** (Figure 1b) it increases up to  $4.72 \text{ \AA}$  due to the bulky sulfur atoms. Interestingly, this steric congestion at the center of the cavity pushes the smaller oxygen atoms away from the center of the macrocycle in the same plane, rather than deviating from a planar conformation. On account of this, **2** attains a rectangular shape in comparison to a square shape of **1**. Therefore, the geometry depends on the type of hetero atoms in the cavity of the macrocycle. The interatomic distance of  $3.1 \text{ \AA}$  between two sulfur atoms is less than their sum of their van der Waals radii ( $3.6 \text{ \AA}$ ), indicative of S–S interactions in the core of the macrocycle. The C–C bond lengths along the perimeter of the macrocycles **1** and **2** exhibit alternate single and double bond characters.

Of particular interest is the intermolecular hydrogen bonding in **2**. Each macrocycle has four acceptor and four donor sites for hydrogen bonding. The *para* fluorine of all four *meso*-pentafluorophenyl rings and the four  $\beta$ -hydrogens of the two thiophenes are involved in C–H $\cdots$ F–C interactions.<sup>11,12</sup> Each molecule forms eight similar hydrogen bonds C4–H4 $\cdots$ F3 ( $2.68 \text{ \AA}$ ,  $171^\circ$ ) with four other neighbors in the same molecular plane (Supporting Information). These C–H $\cdots$ F–C interactions around each macrocycle lead to a well-defined assembly of a two-dimensional grid (Figure 2a). Such hydrogen bonding interactions are very rare in organic fluoro compounds. The voids present in the grid are filled with disordered solvent molecules (Supporting Information).

Similar intermolecular C–H $\cdots$ F–C interactions are also observed in **1**, leading to the formation of a one-dimensional array (Supporting Information). Of more importance is the intermolecular C8–H8 $\cdots\pi$  interactions<sup>13</sup> ( $2.74 \text{ \AA}$ ,  $133^\circ$ ,  $\pi$  orbitals of C6, C7, C8, C9, and O2). It is formed between the  $\beta$ -hydrogen of a furanoid ring from one molecule with the furan  $\pi$  cloud in another molecule. A combination of six such C–H $\cdots\pi$  interactions acts as a driving force for assembling the tetraoxaisophlorin **1** in the form of a cyclic hexamer (Figure 2b). Furthermore, in this hexameric structure, we could also observe three similar F $\cdots$ F interactions (F1 $\cdots$ F10) with a bond distance of  $2.91 \text{ \AA}$ , which is less than the sum of their van



**Figure 2.** Space-filled representations of **2** and **1**. (a) Two-dimensional gridlike structure of **2** formed through C–H $\cdots$ F bonds. Solvent molecules are omitted for clarity. (b) Cyclic hexamer of **1** formed through six C–H $\cdots\pi$  interactions. *meso*-Pentafluorophenyl rings and solvents are omitted for clarity.

der Waals radii ( $2.94 \text{ \AA}$ ).<sup>14</sup> We presume that these F $\cdots$ F interactions cooperate with the C–H $\cdots\pi$  interactions in the crystal packing (Supporting Information).

In conclusion, the synthesis and structural characterization of **1** and **2** provide a novel glimpse into the chemistry of stable isophlorins ever since its hypothesis nearly five decades ago. Their stability can be attributed to the strong electron withdrawing pentafluorophenyl groups on the *meso* carbons of the macrocycle. To the best of our knowledge, C–H $\cdots\pi$  and C( $sp^2$ )–H $\cdots$ F–C( $sp^2$ ) interactions are observed for the first time in large macrocycles to form self-assembled structures. The intermolecular noncovalent interactions of these isophlorins show promise as building blocks to engineer well-defined supramolecular structures.

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**Supporting Information Available:** Experimental details, synthesis of **1–3** and their spectroscopic characterization, and X-ray crystallographic files in CIF for **1** and **2**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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