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Two-electron Oxidation of a Twisted Non Anti-aromatic 40π Expanded Isophlorin

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Abstract. Expanded isophlorins are typical examples for stable anti-aromatic systems. Paratropic ring current effects are observed in their NMR spectra mainly due to their planar conformation. Herein we report the synthesis of the first twisted 40π expanded isophlorin and also its two-electron oxidation to a 38π dication. It sustains the twisted conformation for the 4nπ and (4n+2)π electrons. Due to the non-planar conformation, they do not display ring current effects in their respective ^{1}H NMR spectrum. NICS calculations reveal the non-(anti)aromatic features for the neutral 40π and the 38π dication species.

**Keywords.** Isophlorin; anti-aromaticity; aromaticity; porphyrin; macrocycles; electron transfer

Synthesis of isophlorin, **1**, and its expanded derivatives is actively pursued as targets for stable anti-aromatic macrocycles.[1–6] The macrocyclic structure of an isophlorinoid can be designed from a variety of five-membered heterocyclic rings such as pyrrole, furan, thiophene or selenophene. However, pyrrole based macrocycles can engage their nitrogen(s) in the π-conjugated pathway and exhibit properties similar to that of a porphyrin, **2**. In stark contrast to a porphyrin, expanded porphyrins[7–15] are more vulnerable to redox reactions which are generally proton-coupled electron transfer mechanisms.[16–18] This is aided by the smooth inter-conversion between the imine and amine forms of nitrogen in a pyrrole ring. Avoiding the oxidation of an amine type pyrrole to an imine is crucial to realize tetra-pyrrole isophlorin, **1**. Recently, we demonstrated that a mono pyrrole porphyrin resembles an isophlorin and can be oxidized to the corresponding 18π aromatic dication while retaining the amine-like pyrrole nitrogen.[19] Similarly, non-pyrrolic isophlorinoids exhibit redox properties that are uncommon to aromatic systems.[20] This is evident from their remarkable reversible two-electron ring oxidation into the corresponding aromatic dication.[21] Subtle changes in its electronic properties and structural features accompany this oxidative transformation as observed for anti-aromatic expanded isophlorins. In a peculiar case, a non-planar 32π hexafuran expanded

isophlorin was oxidized to a planar 30π dication.[21] Large expanded porphyrins are destined to adopt figure-of-eight topology owing to their structural flexibility.[22,23] While this is very common amongst porphyrinoids, similar observation has not been frequent for expanded isophlorins.[24] In fact, the only report of a 40π octa-furan[25] expanded isophlorin, **3**, demonstrated a rare planar structure for a macrocycle with eight heterocyclic units (Scheme 1). Herein, we report the synthesis, structural features and the redox properties of a 40π octa-heterocyclic expanded isophlorin derived from a combination of thiophene and furan units.

Earlier, we had synthesized the 20π dithia-dioxaisophlorin, **4**, by an acid catalyzed condensation of thiophene diol with furan subsequently followed by oxidation.[6] Continuing with a similar synthetic strategy, we attempted the synthesis of **5** as a structural isomer of **4**. An equimolar concentration of difurylmethane, **6**, and diol of dithienylmethane, **7**, was catalyzed by $BF_3.OEt_2$ under inert and dark atmosphere followed by oxidation using DDQ (Scheme 2). The MALDI-TOF/TOF mass spectrum of this reaction mixture revealed the formation of a 40π expanded isophlorin, **8**, as the major product rather than the expected 20π isophlorin, **5**. The major product was isolated from silica gel column chromatography in 2.2% yield. High-resolution mass spectrum confirmed the composition of this macrocycle and its structure was elucidated from proton NMR, electronic spectroscopy and single crystal X-ray diffraction. In its proton NMR spectrum recorded at 223 K in $CDCl_3$, **8** displayed only downfield resonances in stark contrast to the symmetrical octa furan
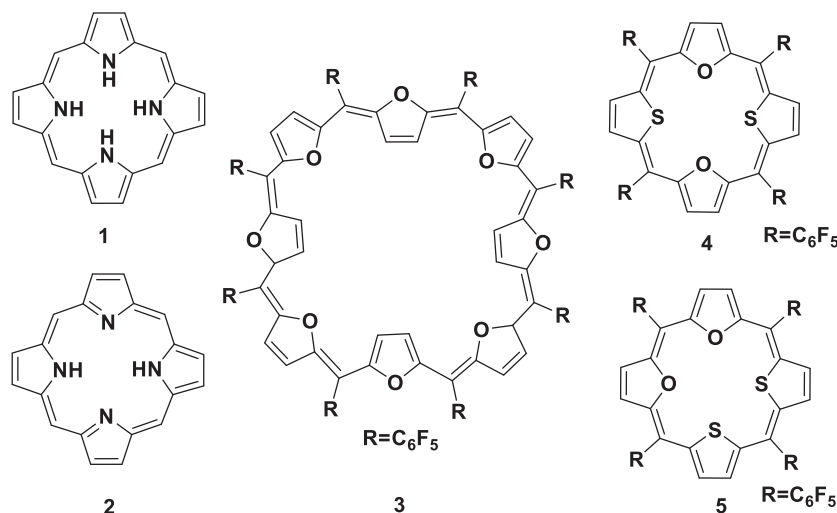
Scheme 1. Structural representations of isophlorin (**1**), porphyrin (**2**), 40π expanded isophlorin (**3**), and isomers of dioxa-dithia isophlorins (**4** and **5**).
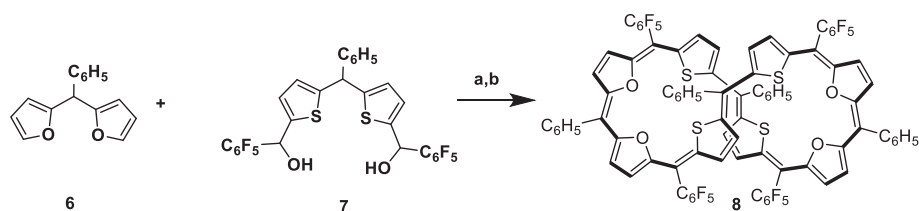
Scheme 2. Synthesis of 40π expanded isophlorin (**8**) with four thiophene and four furan units. (a) 1 equiv. BF_3OEt_2, dry DCM, dark, RT; (b) 3 equiv. DDQ.

expanded isophlorin, **3**. The observed resonances in the region δ 9–6 ppm not only suggested the absence of paratropic ring current effects for the envisaged 40π macrocycle but also its reduced symmetry in comparison to **3**. Variable temperature NMR measurements revealed a well-resolved spectrum at low temperatures, but did not display significant variation in the position of the signals to confirm the absence of solution state dynamics for **8** (Figure 1). In support of this inference from NMR spectroscopy, its electronic absorption spectrum displayed characteristic features of a non-planar macrocycle. The iso-electronic octa furan expanded isophlorin, **3**, was characterized as a planar symmetrical macrocycle with inversion of alternate furan rings as only two singlets were observed in its proton NMR spectrum. Accordingly, **3** exhibited a single and an intense absorption at 535 nm in its electronic absorption spectrum. In contrast, a sharp absorption at 406 nm ($\varepsilon = 1.3 \times 10^5$ $M^{-1}cm^{-1}$) and a broad band at 587 nm (9.3×10^4 $M^{-1}cm^{-1}$) were observed along with a high-energy absorption at 279 nm for **8**. Addition of Meerwein salt[26] to **8**, induced a subtle change in the color of its solution from deep blue to green (Figure 2). The high resolution mass spectrum of this solution displayed m/z (half the molecular weight) value corresponding to its dicationic species, confirming the two-electron ring oxidation of

the macrocycle. The change in color was also marked by significant red shifts in its absorption spectrum. A low intense band at 434 nm (5×10^4 $M^{-1}cm^{-1}$) was accompanied by a intense absorption peak at 793 nm (1.2×10^5 $M^{-1}cm^{-1}$) followed by low energy transitions at 1107 nm (1.0×10^4 $M^{-1}cm^{-1}$) and 1253 nm (5.1×10^3 $M^{-1}cm^{-1}$). Albeit this red shift results from the two-electron oxidation of 40π to 38π dication for the expanded isohplorin, **8**, it did not imply modified structural features. Its ^{1}H NMR displayed sharp signals in the region δ 8.5 to 5.5 ppm at room temperature. While this did not signify a major change to the macrocyclic framework, however, these observations strongly suggested a non-planar conformation for the expanded isophlorin.

Good quality single crystals were grown from CH_2Cl_2/Hexane for **8** and its dication $[\mathbf{8}]^{2+}$. Single crystal X-ray diffraction analysis revealed a figure-of-eight conformation (Figure 3a–b) and represents the first such example for an expanded isophlorin with eight heterocyclic rings.[27] This is remarkable in the context of an octa furan, **3**, and the recently reported octaphyrin dianion with eight pyrrole units,[28] which displayed planar conformation with the inversion of alternate heterocyclic rings. However, the molecular structure of **8** sans any such inversions of heterocyclic rings lead
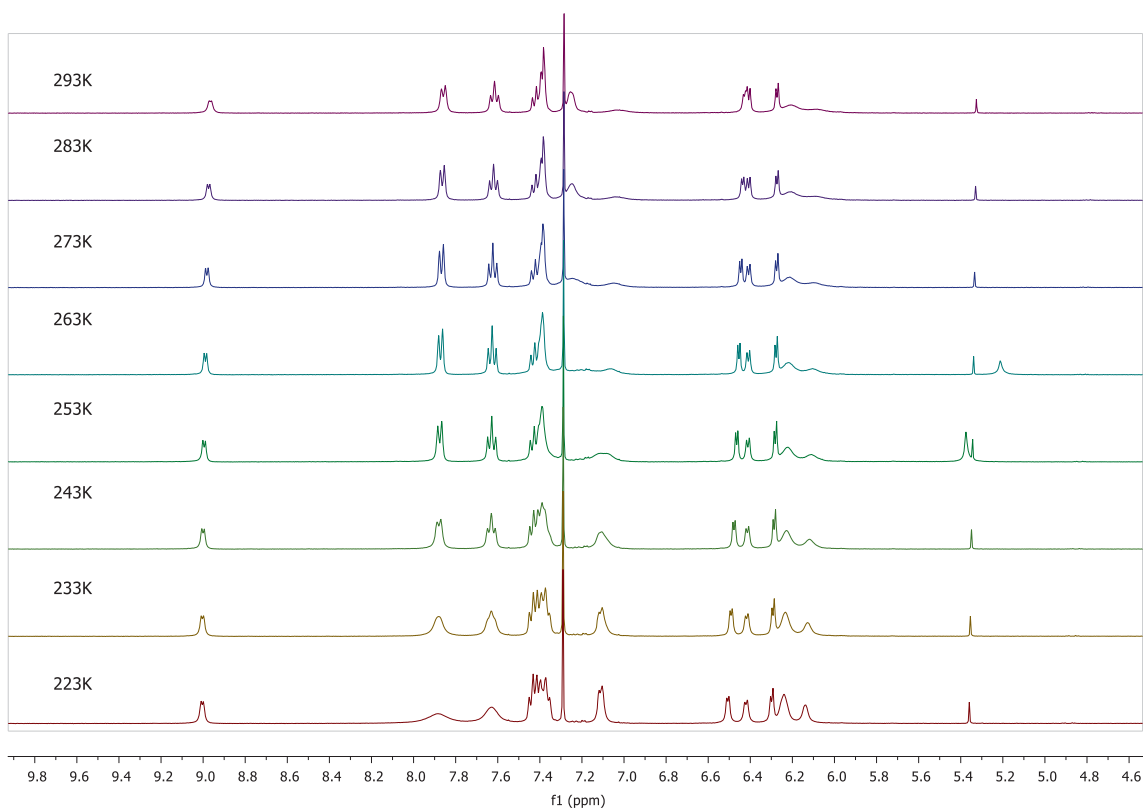
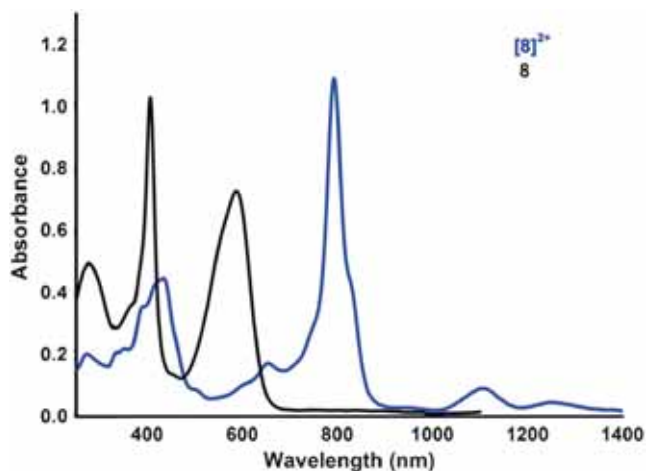**Figure 1.** Variable temperature ^{1}H NMR spectrum of **8** recorded in CDCl$_3$.

Figure 2. Electronic absorption spectra of a 10^{-6}M solution of **8** and [**8**]$^{2+}$ in methylene chloride.

to the twisting of the macrocycle. It can be expected that the molecular twist can happen on a segment with either of the heterocyclic rings. Yet, it was observed that the figure-of-eight conformation was achieved by the crossing of the dithienyl methane units at the center of the macrocycle. The two difuryl methane units were positioned on opposite ends of the structure leading to two isophlorin-like pockets similar to the target molecule, **5**. All the heterocyclic units have a uniform orientation such that the heteroatoms are directed towards

the center of the macrocyclic cavity. Compared to other pyrrole based twisted octaphyrins,[28,29] sulfur atoms of the overlapping thiophene rings were found to be farther away from the macrocyclic center to appear like a tweaked figure-of-eight conformation. The molecular structure of the dication, [**8**]$^{2+}$, retained the same conformation as that of the free base. Similar to our earlier reports on the oxidation of 4nπ systems, two molecules of [SbCl$_6$]$^-$ were found for each macrocycle, confirming the dicationic form of the macrocycle. Oxidation of octafuran, **3**, or deprotonation of octaphyrin was conducive enough to uncurl the macrocycle into a planar conjugated system. But the presence of two sets of dithienyl methane and difuryl methane tend to stabilize the twisted conformation in stark contrast to the homogenous distribution of heterocyclic units. Further, we employed quantum chemical calculations to estimate the Nucleus Independent Chemical Shift (NICS)[30] values for both **8** and [**8**]$^{2+}$. NICS is a commonly employed computational tool to estimate the magnitude of a π-delocalization in conjugated macrocycles. The computed NICS values of $+3.5131$ (on individual centers $+3.9011$, 3.8416) and -7.7568 (on individual centers -5.913, -6.0516) for **8** and [**8**]$^{2+}$ clearly suggested their non anti-aromatic and aromatic characteristics, respectively. These values are in complete agreement with the spectroscopic and structural features as described above.
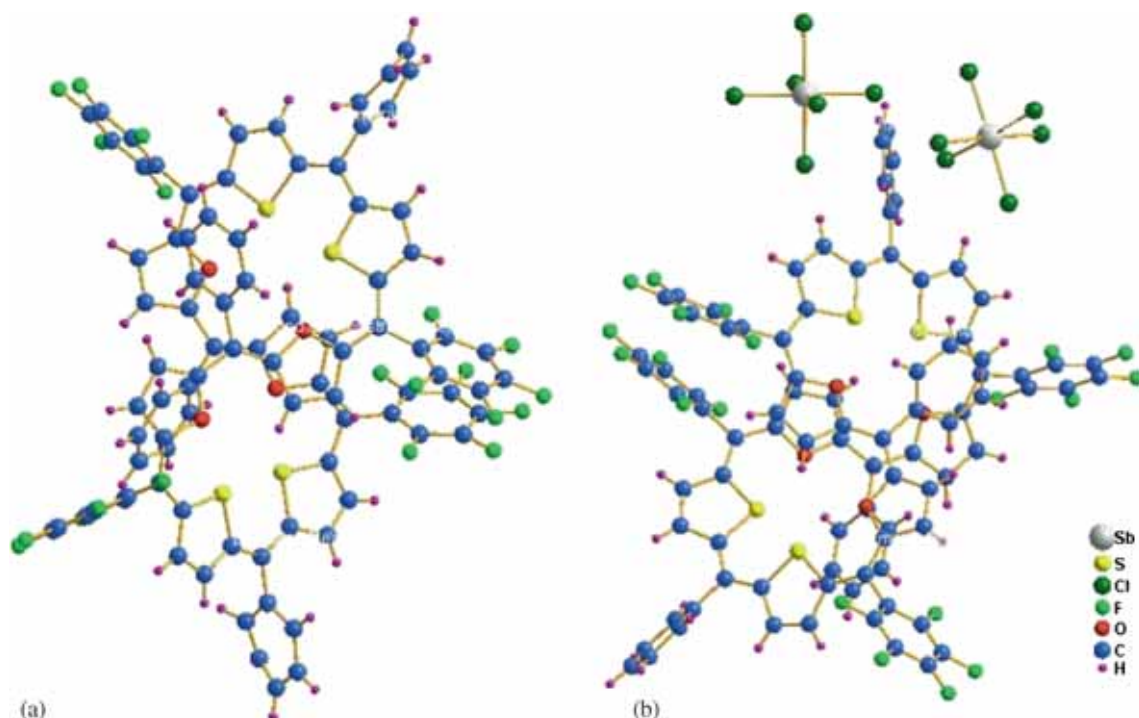
Figure 3. (**a–b**). Molecular structure of (a) **8** [CCDC NO. 1502326] and (b) **[8]$^{2+}$** [CCDC NO.1502347] as determined from single crystal X-ray diffraction analysis.

In summary, we have synthesized and characterized the first 40π expanded isophlorin with a figure-of-eight conformation. The composition of the hetero-cyclic units seems to be crucial to the topology of the macrocycle. It undergoes typical two-electron oxida-tion, as expected of $4n\pi$ systems, without undergoing a structural transformation into a planar macrocycle. Spectroscopic data and computational studies help us to conclude that the macrocycle is devoid of ring current effects and hence they are non (anti)aromatic in nature. Upon twisting, the macrocycle shows a twin pocket similar to the targeted 20π isophlorin **5** and seems to be an ideal binding site for metal ions. More work in this direction is under progress in our laboratory.

Supplementary Information (SI)

Details of synthesis and spectroscopic characterization of **8** and [**8**]$^{2+}$ are available at www.ias.ac.in/chemsci.

Acknowledgements

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27. (a) Crystal data for **8**: C_{88} H_{36} $F_{20}O_4$ S_4 2(O) (M_r= 1697.41), orthorhombic, space group ($P1$), a=13.0601(19) Å, b=13.0601(19) Å, c=28.618(4) Å, a=90 β=90 γ=90 V=7806(2) Å^3, Z=4, T=100(2)) K, D_{calcd}=1.444 g cm^{-3}, R1=0.0957, R_w=0.2857(9498), GOF=1.048. (b) Crystal data for $[8]^{2+}$: $C_{88}H_{36}F_{20}O_4S_4$, 2(Cl_6Sb) (M_r=2334.33), space group=Triclinic (P-1), a=18.012(3) Å, b= 18.338(2) Å, c=19.375(3) Å, a=92.256(3) β=99.338(3) γ=111.588(3) V=5837.6(15) Å^3, Z=4, T=100 K, D_{calcd}=1.328 g cm^{-3}, R1=0.0741(13194), Rw=0.2496 (29298), GOF=0.707
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