Radicals

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An Amphoteric Switch to Aromatic and Antiaromatic States of a Neutral Air-Stable 25π Radical[**]

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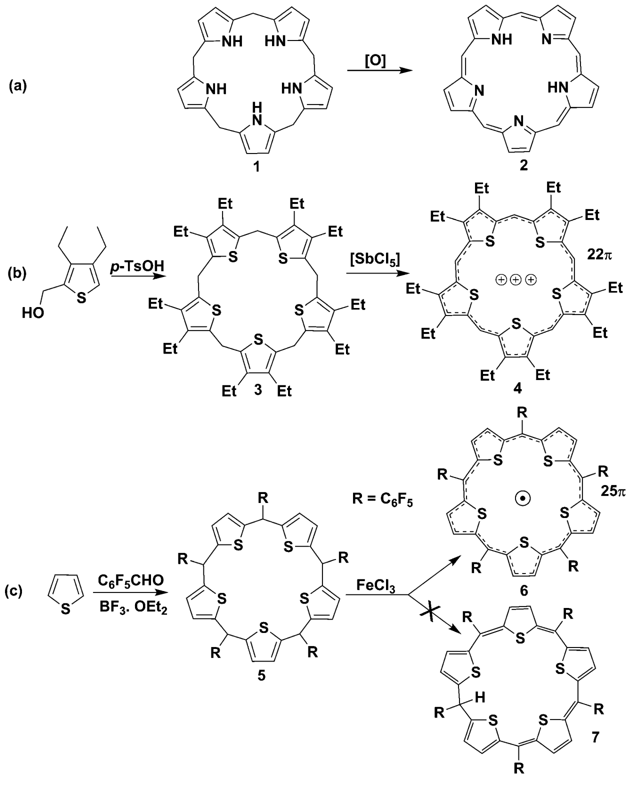
Abstract: *Ever since the discovery of the trityl radical, isolation of a stable and neutral organic radical has been a synthetic challenge. A (4n+1)π open-shell configuration is one such possible neutral radical but an unusual state between aromatic (4n+2)π and antiaromatic (4n)π electronic circuits. The synthesis and characterization of an air- and water-stable neutral 25π pentathiophene macrocyclic radical is now described. It undergoes reversible one-electron oxidation to a 24π antiaromatic cation and reduction to a 26π aromatic anion, thus confirming its amphoteric behavior. Structural determination by single-crystal X-ray diffraction studies revealed a planar configuration for the neutral radical, antiaromatic cation, and aromatic anion. In the solution state, the cation shows the highest upfield chemical shift ever observed for a 4nπ system, while the anion adhered to aromatic nature. Computational studies revealed the delocalized nature of the unpaired electron as confirmed by EPR spectroscopy.*

Aromatic and antiaromatic states imply a two-electron redox process through a transient $(4n+1)\pi$ radical. Sustaining open-shell configurations is a hard task owing to their short lifetime, which thwarts their isolation and characterization. After the discovery of the trityl radical, only a few others are known to be stable enough to persist as a radical.[1] Neutral radicals have attracted interest not only from stability as such, but also for applications in organic radical batteries.[2] We report the synthesis, isolation, characterization, and the redox chemistry of a stable penta-thiophene 25 π-electron radical. Porphyrinoids have attracted wide interest for their intriguing structural features and tunable electronic properties.[3] In an elegant study, Vogel and co-workers revealed the considerable variation in the electronic properties of a porphyrin upon replacing all of the pyrroles by furan sub-units. The 20π antiaromatic macrocycle, tetraoxaisophlorin, was referred as a "pseudo-metal"[4] for its ability to form aromatic dicationic species upon oxidation by mineral acids. However, a similar exchange of pyrrole by thiophene in a pentaphyrin frustrates the macrocycle to complete conjugation (Scheme 1).



Scheme 1. a) Oxidation of penta-pyrrole to 22π pentaphyrin.[5] b) Oxidation of penta-thiophene to 22π trication.[6] c) One-pot synthesis of 25π radical from thiophene and pentafluoro- benzaldehyde.

Oxidation of **1** to pentaphyrin **2** (Scheme 1a) is enabled by the transformation of nitrogen from amine to imine within the macrocyclic framework.[5] In contrast, the pentathiophene **3** forms a completely conjugated 22π trication, **4**, upon oxidation (Scheme 1b).[6] Recent reports highlight the unexplored facet of the electron-transfer process in expanded porphyrins[7] and thiophene-based π-conjugated macrocycles.[8] Completely conjugated macrocyclic polythiophene undergoes systematic π-oxidation to form radical cation or bipolaron species. Spectroscopic studies revealed temperature-dependent dimerization of the isolated radical cation into a polaron pair, as expected of radical species. Our own recent report confirms reversible two-electron redox reaction of antiaromatic expanded isophlorins through electron-trans-

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fer reagents.[9] These results encourage the possibility of a 25π radical crucial to transform an unconjugated **3** into a conjugated macrocycle.

The phenomenal role of pentafluorobenzaldehyde in the synthesis of π-conjugated macrocycles has been illustrated by the one-pot synthesis of porphyrinoids under oxidative conditions.[10] Anticipating analogous macrocycles under identical reaction conditions, a catalytic amount of boron trifluoride etherate was added to equimolar ratio of thiophene and pentafluoro benzaldehyde in dichloromethane (Scheme 1 c). After stirring for an hour, the reaction mixture was exposed to air and $FeCl_3$ was added, with stirring continued for additional one hour. The MALDI-TOF mass spectrum of this reaction mixture revealed macrocycles containing four to ten thiophene sub-units. Separation of the mixture by column chromatography led to easy isolation of macrocycles with four, five, six, and eight thiophene subunits. Macrocycles with seven, nine, and ten thiophene subunits were identified in relatively poor yields. Our analysis of the 20π tetrathiaisophlorin[11] and 30π hexathia hexaphyrin[12] were similar to earlier reports. A green-colored solution obtained by chromatographic separation showed *m*/*z* value of 1304.8992 in its high-resolution mass spectrum (see the Supporting Information). A unit mass less than the expected *m*/*z* value of a semi-conjugated macrocycle **7** ($C_{55}H_{11}F_{25}S_5$: calcd. 1305.9065) suggested the formation of the radical **6**$^{\bullet}$ ($C_{55}H_{10}F_{25}S_5$: calcd. 1304.8987) upon oxidation of **5**. Evaporation of solvent yielded a green solid with metallic sheen, the ^{1}H NMR spectrum of which did not display any signal corresponding to the macrocycle, either at room temperature or at low temperature. EPR spectrum of **6**$^{\bullet}$ recorded at room temperature and at 77 K displayed a singlet with $g = 2.0026$, characteristic of a radical having an unpaired electron ($S = 1/2$). It was found to be stable even upon exposure to ambient atmosphere for several months. Thermogravimetric analysis confirmed its high thermal stability up to 300 °C (see the Supporting Information).

Appropriate redox reagents were employed to confirm the radical behavior of **6**$^{\bullet}$ by deriving the corresponding monocation and monoanion (Figure 1). Meerwein salts, such as $[Et_3O]^+[SbCl_6]^-$, act as an effective one-electron oxidizing agent for π-conjugated systems.[13] Addition of this salt to **6**$^{\bullet}$ in dichloromethane immediately induced a color change from a green to brownish solution. Addition of the brownish solution to cooled diethyl ether yielded dark-colored crystals of **6**$^+$. ^{1}H NMR spectrum obtained by dissolving the crystals of **6**$^+$ in CD_3CN displayed a singlet at $\delta = -6.77$ ppm at 293 K, while it was further upfield-shifted to −7.86 ppm at 230 K (see the Supporting Information). The remarkable paratropic ring current effect expected of a 24π antiaromatic cation confirmed the one-electron oxidation of the radical. Such a strong upfield chemical shift is the highest ever to be recorded for any 4*n*π macrocycle to date, which further validated a planar confirmation of **6**$^+$ in solution state. The radical **6**$^{\bullet}$ was also subjected to one-electron reduction by potassium superoxide (KO_2) in the presence of 18-crown-6 (18C6). Addition of KO_2 to a solution of **6**$^{\bullet}$ in DMSO induced a quick change in the color of the solution from green to pink. ^{1}H NMR spectrum obtained by mixing **6**$^{\bullet}$, KO_2, and 18C6 in deuterated DMSO displayed a singlet for **6**$^-$ at 11.15 ppm. Such a downfield shift confirmed the diatropic ring current effect of the 26π aromatic anion obtained by the one-electron reduction of the radical **6**$^{\bullet}$. The independent chemical transformation of the radical **6**$^{\bullet}$ into antiaromatic cation **6**$^+$ and aromatic anion **6**$^-$ could be demonstrated by contrasting ring current effects in their respective ^{1}H NMR spectrum.

Electronic absorption and cyclic voltammetric studies validated the redox process for the radical **6**$^{\bullet}$ (Figure 2). The neutral radical **6**$^{\bullet}$ exhibited an intense absorption at 470 nm ($\varepsilon = 195\,000$) in dichloromethane. Upon oxidation, the brownish color solution of **6**$^+$ displayed a red-shifted absorption at 513 nm (150 000) with relatively decreased intensity, followed by characteristic weak and broad absorption, in the region between 900–1000 nm, for antiaromatic macrocycles.[14] The pink-colored solution of anion **6**$^-$ shows an intense red-shifted absorption at 542 nm (270 000) with a Q-like band at 730 nm (24 000), signifying the aromatic characteristics of the reduced

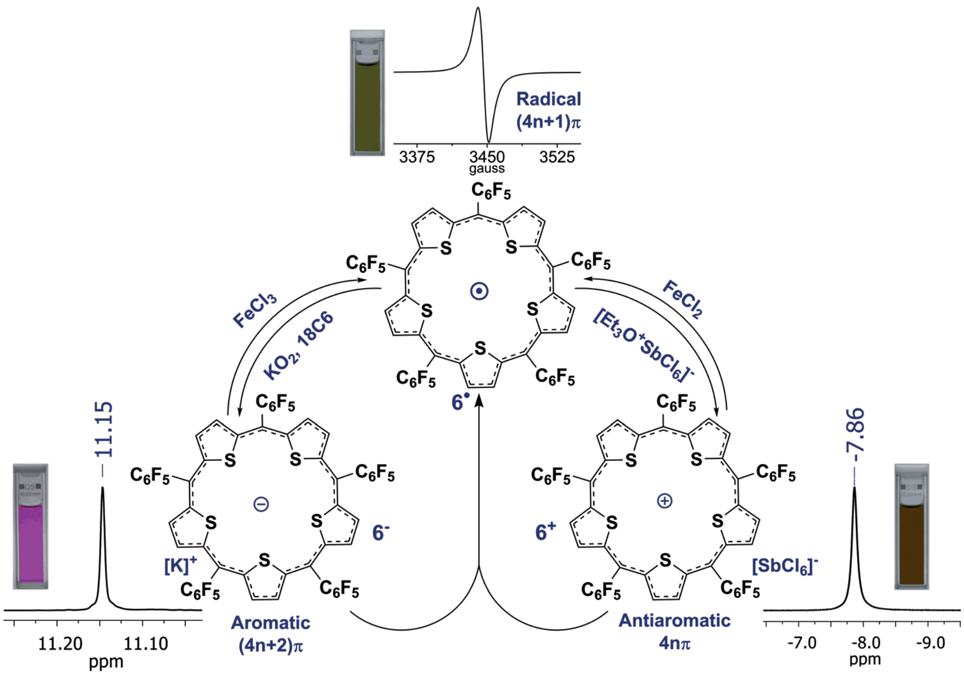

Figure 1. Amphoteric properties of **6**$^{\bullet}$ along with spectroscopic characteristics of **6**$^+$ and **6**$^-$. The EPR signal (above) for radical **6**$^{\bullet}$ and the ^{1}H NMR signals for **6**$^-$ (left) and **6**$^+$ (right) along with their respective color in the solution state.

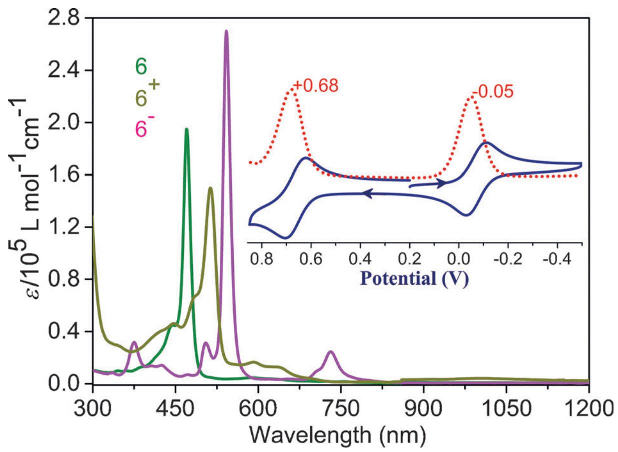

Figure 2. Changes observed in the electronic absorption spectra of 10^{-6} M **6**$^{\bullet}$ upon its reduction to **6**$^{-}$ (in DMSO) and oxidation to **6**$^{+}$ (in CH_2Cl_2). Inset: the first reduction and oxidation observed in the cyclic voltammogram (blue) and differential pulse voltammogram (red) for **6**$^{\bullet}$ recorded in CH_2Cl_2 with tetrabutylammonium perchlorate as the supporting electrolyte.

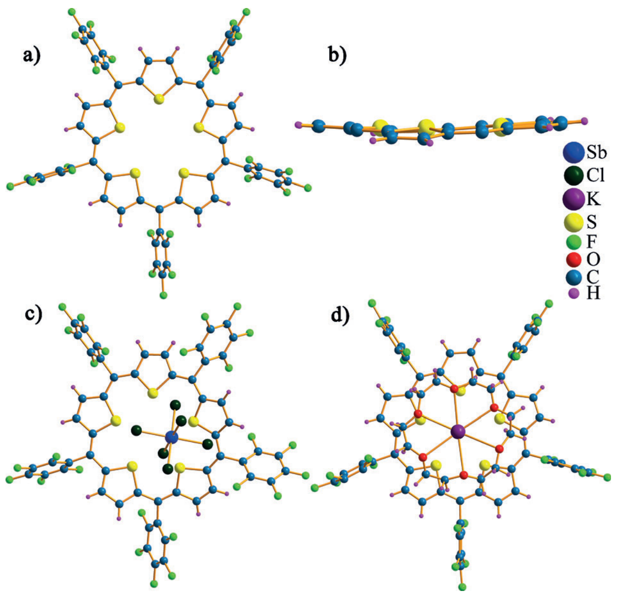

Figure 3. Molecular structures determined from single-crystal X-ray crystallography. a) Top view of **6**$^{\bullet}$. b) Side view of **6**$^{\bullet}$ (pentafluorophenyl rings are omitted for clarity). The pentathiophene macrocycle retains the planar structure for both c) cation **6**$^{+}$ with hexachloroantimonate counteranion and d) anion **6**$^{-}$ with K^{+}(18C6) countercation.

radical. More importantly, we employed electronic absorption studies to study the reversible nature of the redox process upon oxidation of **6**$^{-}$ and reduction of **6**$^{+}$ with iron salts. Addition of $FeCl_3$ to **6**$^{-}$ and addition of $FeCl_2$ to **6**$^{+}$ changed the color of the respective solutions to green with a simultaneous shift in its absorption corresponding to that of radical **6**$^{\bullet}$. Combining **6**$^{+}$ and **6**$^{-}$ lead to a comproportionation reaction, as observed by the single absorption corresponding to **6**$^{\bullet}$, demonstrating their ability to act as a mutual redox couple. The mutual neutralization of the ionic species supported the high stability of the neutral radical. Cyclic voltammetry studies (Figure 2) gave decisive evidence for the amphoteric nature of the radical **6**$^{\bullet}$. In dichloromethane, it exhibits one reduction wave at −0.05 V and four oxidation waves in the region between 0.6–1.5 V. The E^{sum} obtained from the numerical sum of first E^{ox} and E^{red} is attributed to the ease of amphoteric behavior of a hydrocarbon.[15] An estimated E^{sum} value of 0.73 V from the first reduction (−0.05 V) and oxidation (+0.68 V) proved the facile amphoteric nature of the radical. It is one of the lowest values compared to previous reports for radicals.[1f]

Finally, we established the molecular structures of **6**$^{\bullet}$, **6**$^{+}$, and **6**$^{-}$ by single-crystal X-ray diffraction analysis (Figure 3) to confirm the absolute stability of the radical and its ionic derivatives under ambient conditions.[16] They displayed an unprecedented planar conformation with respect to the five thiophenes. Sulfur atoms of all the five thiophenes point towards the center of the macrocycle. This structure is the first example belonging to planar meso-phenylpentaphyrin class of macrocycles that lack inversion of the heterocyclic units to emphasize the effective delocalization of the π-electrons for the additional stability of the radical. Similar macrocycles with pentapyrrole derivatives undergo ring inversion followed by fusion, leading to non-planar conformation.[17] The near orthogonal orientation of the pentafluorophenyl rings with respect to the plane of the macrocycle in **6**$^{\bullet}$ facilitates the steric-hindrance-induced prevention of π stacking to diminish the possible interaction between the unpaired electrons. In contrast, planar π radicals can dimerize through π-stacking, which can form a singlet or triplet spin state.[1b,18] Good-quality single crystals of **6**$^{+}$ grown from acetonitrile also exhibited a flat structure in the solid state. Hexachloroantimonate was found to be associated with the cationic macrocycle to justify the adduct nature of the oxidized macrocycle. Single crystals of the reduced derivative **6**$^{-}$ grown from DMSO were also found to possess a planar structure with potassium bound by 18C6 as the countercation. These molecular structures, in combination with other spectroscopic data mentioned above, unambiguously confirmed the one-electron ring oxidation and reduction of the radical **6**$^{\bullet}$.

We performed unrestricted DFT calculations (UB3LYP/6-31G (d,p)) in an effort to understand the unusual high stability of this open-shell species **6**$^{\bullet}$. The calculations implied the unpaired electron density to be encompassed over the cyclic framework of **6**$^{\bullet}$ (see the Supporting Information). Anisotropy of the induced current-density (AICD)[19] plot for **6**$^{\bullet}$ displayed an anticlockwise ring current favoring the antiaromatic character of the pentaphyrin. The effect of delocalization for **6**$^{\bullet}$ was further supported by the computed nucleus-independent chemical shift[20] (NICS(0)) value of +14.66 ppm. A NICS(0) value of +37.50 ppm for the cation **6**$^{+}$ is the highest-ever computed value for antiaromatic species, equally matched by a strong paratropic ring current effect in its ^{1}H NMR spectrum. Furthermore, the smallest HOMO–LUMO gap of 1.04 eV, optically dark NIR states at 2520 nm,[14] and anticlockwise ring current flowing only through carbon atoms of thiophene and meso positions was observed for the highly stable antiaromatic nature of **6**$^{+}$. A negative NICS(0) value of −14.96 ppm, relatively high HOMO–LUMO gap of 2.24 eV, and clockwise ring currents in its AICD plots was observed to confirm the aromatic property of **6**$^-$. TDDFT calculations also supported the experimental findings.

In conclusion, we have established a straightforward synthesis of the most stable organic radical from commercially available precursors. It exhibits a property very similar to that of metals with multiple oxidation states. The amphoteric nature of a radical has been established by electrochemical and chemical process. For the first time we have characterized a neutral radical and its corresponding oxidized and reduced forms in solution and solid states. Such stable organic radicals can be expected to play a significant role in organic catalysis and in the development of organic semiconductors.

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