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Synthesis and Reactions of 20 π-Electron β-Tetrakis(trifluoromethyl)-*meso*-tetraphenylporphyrins

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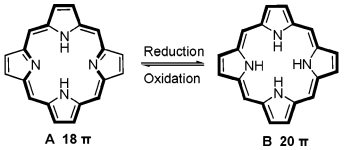
Porphyrin and their analogues usually have a stable aromatic $(4n + 2)$ π-electron system. Porphyrin itself shows aromatic behavior with an 18 π-electron main conjugation pathway in the molecule and has been intensively investigated.[1] However, porphyrin derivatives with $4n$ π-electron delocation pathways have been little explored owing to their synthetic difficulty,[2,3] and the majority of them are expanded porphyrins[3] because the difference between resonance stabilization energies of $4n$ and $(4n + 2)$ π-electron systems decreases for larger values of n.[4] To the best of our knowledge, the synthesis of 20 π-electron *N,N′*-dihydroporphyrin (isophlorin) **B**, referred to for the first time by Woodward during the synthesis of chlorophyll about half a century ago,[5] has represented a challenge for porphyrin chemistry and remained elusive thus far because of its intensive tendency to undergo a two-electron oxidation and deprotonation to form its corresponding 18 π-electron aromatic porphyrin **A**.(Scheme 1) Herein, we report the isolation and structural characterization of the 20 π-electron nonaromatic isophlorin **2** and its N-methylation reactions.

During our ongoing efforts in synthesis and application of perfluoroalkylated porphyrins,[6] a facile and effective synthesis of the isophlorin **2** was achieved with the accidental discovery of a ready reduction of Cu(II) β-tetrakis(trifluoromethyl)-*meso*-tetraphenylporphyrin (**Cu1**).[7] When adding activated zinc powder into a DMSO solution of **Cu1** at room temperature under nitrogen, the color of the contents changed form green to brown after 1 h. TLC indicated almost complete consumption of the starting porphyrin and formation of a main orange product **2**. (Scheme 2) It was relatively air stable[8] to be successfully isolated and thoroughly characterized, although being easily reoxidated to free-base β-tetrakis(trifluoromethyl)-*meso*-tetraphenylporphyrin ($\mathbf{H_21}$) with 2,6-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

X-ray crystal diffraction analysis of **2** (Figure 1) elucidated that it was a 20 π-electron isophlorin with a highly distorted skeleton that displays a nonplanar saddle conformation.[9] The average displacement for the β-carbons from the least-squares plane of the *meso*-carbon atoms, which can be used to evaluate the magnitude of distortion in the macrocycle, was 1.36 Å for **2** in contrast with 0.89 Å for **Cu1**.[8] It is also a manifestation of serious distortion of the macrocycle that the pyrrole rings with trifluoromethyl groups and pyrroline rings without trifluoromethyl groups are titled on average by 69.7° and 33.5°, respectively, out of the least-squares plane. The remarkably strong twisting of the pyrrole units might be attributed to considerable steric congestion present between meso and β substituents, as well as NH-hydrogen atoms. In addition, an expected feature exhibited in the structure of **2** is that clear C−C bond-length alternation is observed around the macrocycle periphery, which dramatically contrasts with its corresponding 18 π-electron aromatic porphyrin **Cu1**.[8]

Scheme 1. Redox Transformation between 18 and 20 π-Electron Porphyrin Core



Scheme 2. Reduction Reaction of **Cu1** with Zn

Spectroscopic data obtained indicate that **2** is a nonaromatic system. NMR spectrum of **2** are in sharp contrast with that of its oxidative 18 π-electron aromatic counterpart $\mathbf{H_21}$.[8] In the ^{1}H NMR spectrum of **2**, the pyrroline β-protons are shifted obviously upfield to 6.87 ppm. A similar but weaker effect was observed for peaks located at 7.10, 7.26, and 7.34 ppm, which were identified as belonging to the *meso-o*, *p*, and *m*-phenyl protons, respectively. Two singlets at 8.40 and 9.87 ppm were considered in accord with the far downfiled-shifted NH-protons of pyrroline rings without trifluoromethyl groups and pyrrole rings with trifluoromethyl groups, respectively. The ^{19}F NMR chemical shift of **2** were shifted upfield by about 5 ppm compared to that of $\mathbf{H_21}$. These spectra shift can be reasonably interpreted in terms of collapse of the diatropic ring current and almost complete conformation-induced loss of the paratropicity in the porphyrin macrocycle.[10] The UV−vis spectra of **2** is also quite characteristic, which shows a

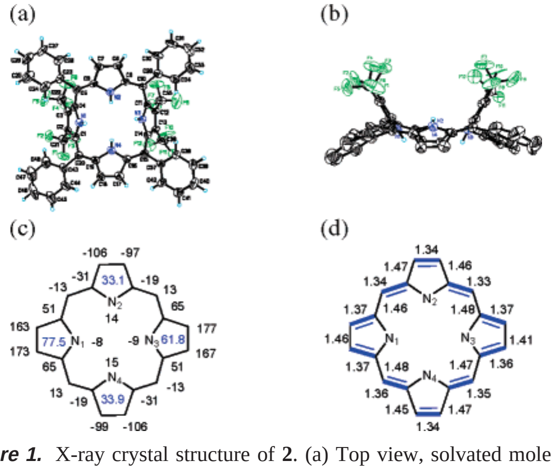


Figure 1. X-ray crystal structure of **2**. (a) Top view, solvated molecules have been omitted for clarity; (b) side view, solvated molecules and hydrogen atoms have been omitted for clarity, with the exception of the NH groups; (c) displacements (in 0.01 Å units) of the core atoms from their least-squares plane of the *meso*-carbon atoms (black) and torsion angles between pyrrole units and the least-squares plane (blue); (d) bond distances (in Å) in the core.

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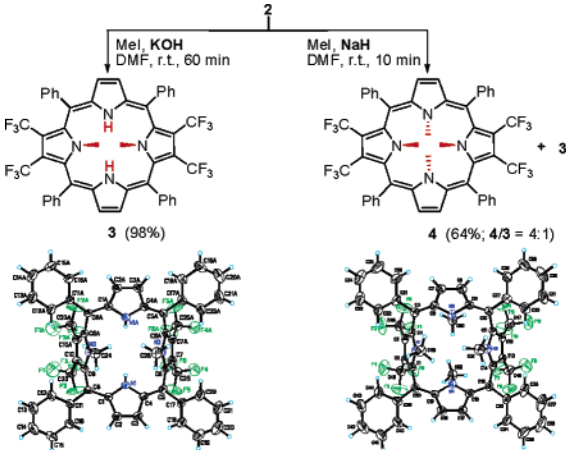
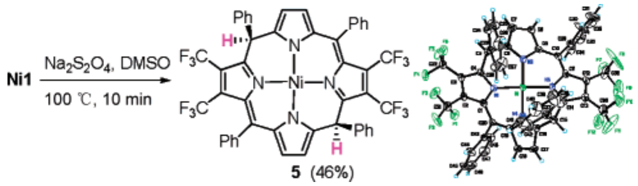
Scheme 3. N-Methylation Reactions of the Isophlorin **2**



Scheme 4. Reduction Reaction of **Ni1** with $Na_2S_2O_4$



broad single Soret bond at 418 nm and no Q-bands are observed.[8] All these features are well consistent with that of recently reported $4n$ π-electron nonaromatic porphyrinoids.[2c−e,3b,g]

With this novel isophlorin **2** in hands, we then subjected it to N-methylation reactions. (Scheme 3) It was found that the base used exercised a great influence on the reaction. When KOH was used, treatment of **2** with MeI in DMF at room temperature for 1 h resulted in the formation of N-dimethylated isophlorin **3** in quantitative yield. By contrast, the reaction utilizing NaH as a base under similar conditions proceeded quickly and led to a 4:1 ratio of N-tetramethylated isophlorin **4** to **3** within 10 min in good yield. Extended reaction time proved invalid for complete conversion of **3** into **4**. The ratio was essentially retained even after longer reaction time (12 h). The structures of **3** and **4** were confirmed by X-ray crystal diffraction analysis, and all display a similar nonplanar seriously distorted saddle skeleton and analogous spectroscopic characteristics with **2**, indicating their 20 π-electron nonaromatic nature. However, they are more air stable than **2** likely because of mutual repulsion of N-methyl groups that significantly hinders the rotation of the pyrrole units into the near-planar conformation required for oxidation.

Subsequent investigation on the former reduction reaction revealed that Ni(II) β-tetrakis(trifluoromethyl)-*meso*-tetraphenylporphyrin (**Ni1**) was not an appropriate substrate for the reduction reaction under similar conditions, resulting in complete recovery of the starting porphyrin. Raising the reaction temperature led to serious degradation of porphyrins. To our surprise, when $Na_2S_2O_4$ was used instead of activated zinc powder at 100 °C for the reaction, an interesting porphodimethene **5** was obtained in moderate yield, which was convincingly determined by spectroscopic data obtained including X-ray crystal diffraction analysis. (Scheme 4) It was air stable and stable against oxidation with DDQ, which appears understandable if the energy required for interrupting the porphyrin macrocycle conjugation can be offset by the relief of macrocycle strain in highly congested porphyrin by its conversion into the corresponding porphydimethenes.[11]

In summary, we have successfully isolated and thoroughly characterized the 20 π-electron nonaromatic isophlorin **2** and its N-methylated analoguous **3** and **4**. When **Ni1** was used in the reaction with $Na_2S_2O_4$ as a reductant at 100 °C, porphydimethene **5** was obtained. It is considered that the four strongly electron-withdrawing bulky trifluoromethyl groups at β positions play a very important role in the reaction on the basis of the observation that 5,10,15,20-tetraphenylporphyrin, 5,10,15,20-tetrakis(4-trifluoromethylphenyl)porphyrin, 2-trifluoromethyl-5,10,15,20-tetraphenylporphyrin, 2,3,12,13-tetrabromo-5,10,15,20-tetraphenylporphyrin, or 5,15-bis(trifluoromethyl)-10,20-diphenylporphyrin did not show the analogous reduction reactions under similar conditions. Further studies on the reduction reactions are now in progress.

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Supporting Information Available: Experimental details, characterization data, and crystallographic data in CIF format for **2**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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