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A Structural Isomer of Nonaromatic Porphyrin: Preparation of 20π-Conjugated Porphycene Based on Electronic Perturbation

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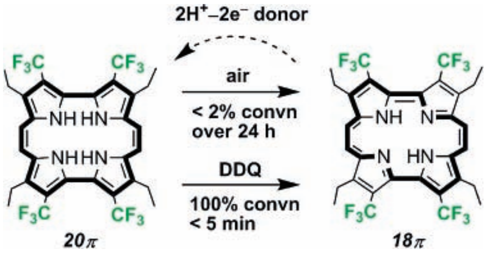
ABSTRACT



A porphycene having four CF_3 groups at the β-pyrrolic positions affords a stable 20π-conjugated form in the presence of a $2H^+$–$2e^-$ donor due to the high redox potential of the tetrapyrrole ring framework. No visible band in the UV–vis spectrum and the highly ruffled structure determined by X-ray crystallography support its nonaromatic character. The ethylene bridge moiety in the 20π-conjugated framework displayed the olefinic reactivities.

The π-conjugation system of porphyrin, a tetrapyrrolic 18π-conjugated macrocycle, is controlled by designing the framework structures, for example, peripheral substitutions,[1] changes in the arrangement of pyrrole units including ring expansion/contractions,[2] and introducing non-pyrrolic units.[2] However, the structure-modified porphyrinoids, in many cases, also maintain aromaticity, that is, the $(4n + 2)$ π-conjugation system. In contrast, the preparation of porphyrinoids with $4n$ π-conjugation system, namely, “nonaromatic porphyrinoids”, is a unique approach to dramatically alter the π-conjugation behaviors of a tetrapyrrolic macrocycle.[3] The nonaromatic porphyrinoid being most structurally close to porphyrin is isophlorin, a tetrapyrrole with a 20π-conjugated character, first reported by Woodward.[4] Generally, the isolations of 20π-conjugated porphyrinoids are rather difficult because of their tendency to be oxidized to the corresponding 18π-conjugated form, unless the nitrogens on the pyrrole rings are alkylated or replaced with oxygen or sulfur atoms.[5] However, a recent report of a 20π-conjugated Cu−porphyrin having four CF_3 and phenyl groups in the framework[3] suggests the possibility of isolating 20π-conjugated porphyrinoids by well-considered electronic/structural modulations on the framework. We now report the chemistry of the 20π-conjugated porphycene with CF_3 groups at the β-pyrrolic positions, **1**, shown in Scheme 1, together with the 18π-conjugated form, **2**.

Porphycene, a structural isomer of porphyrin pioneered by Vogel,[6] is normally synthesized by McMurray coupling

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[1] *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 1.

[2] (a) Sessler, J. L.; Seidel, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 5134−5175 and references therein. (b) *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 2.

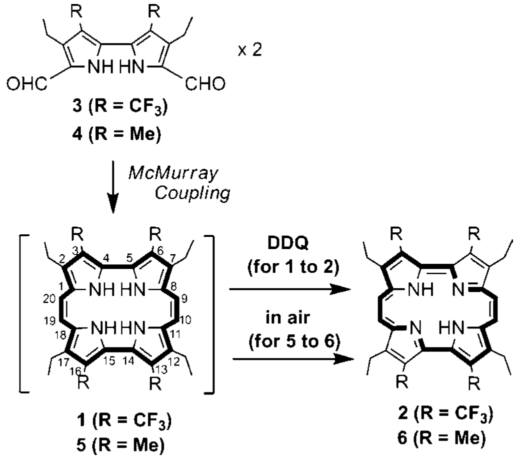
[3] The selected papers for $4n$ π-conjugated porphyrins are listed in: Liu, C.; Shen, D.-M.; Chen, Q.-Y. *J. Am. Chem. Soc.* **2007**, *129*, 5814−5815 and references therein.

[4] Woodward, R. B. *Angew. Chem.* **1960**, *72*, 651−652.

[5] Pohl, M.; Schmickler, H.; Lex, J.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1693−1697.

10.1021/ol7025087 CCC: $37.00

Scheme 1. Synthesis of Porphycene



of two 5,5′-formylbipyrroles (**3** or **4** in Scheme 1). During the coupling of **4** (R = Me), the presumed coupling product **5**, a 20π-conjugated form, is readily oxidized to **6** in air, whereas the formation of a CF$_3$-introduced porphycene **2** requires the addition of DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) to the reaction mixture.[7] On the basis of this fact, we can expect that the 20π-conjugated porphycene would be stabilized by controlling the electronic configurations of the porphycene framework. This is another strategy to prepare a structural isomer of isophlorin such as pyrrolophanediene porphycene.[8,9]

The isolation of the 20π-conjugated porphycene **1** from the reaction mixture of McMurray coupling of **3** was impossible due to the difficulty in the separation of many kinds of byproducts. Therefore, we attempted the reaction of **2** with some reducing reagents to yield the pure **1**. Upon the addition of 2.0 equiv of tributyltin hydride (Bu$_3$SnH) and 2.0 equiv of trifluoroacetic acid (TFA) to the solution of **2** in dry CH$_2$Cl$_2$ at 25 °C, the typical absorption bands of **2** around 380, 600, and 720 nm decreased over 24 h along with the growth of a new band around 300 nm (Figure 1). In the absence of TFA, no such spectral change was observed. This finding indicates that both two protons and two electrons are required for the reaction to proceed. Similar spectral changes were also observed in the reaction with sodium dithionite in water/THF (25% (v/v)) (Scheme 2), in which water would function as a proton donor. The disappearance of the absorption bands suggests a significant perturbation to the electronic states in the 18π-aromatic ring system.[10]

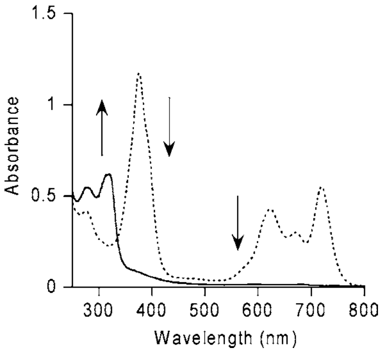
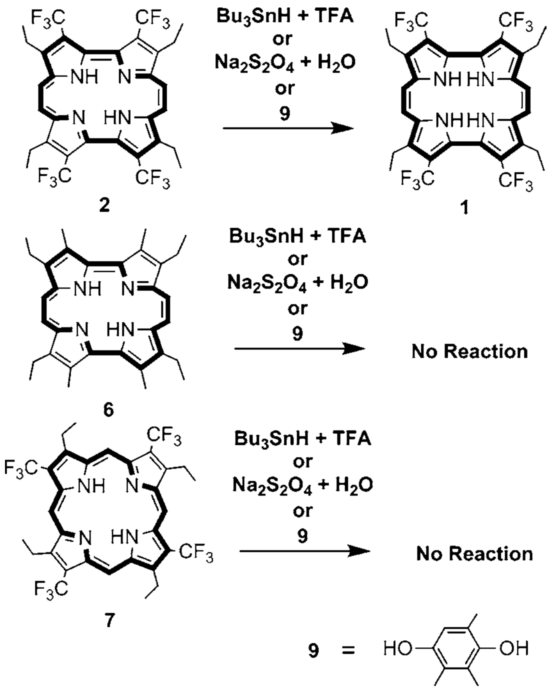


Figure 1. UV−vis spectral changes during the reaction of **2** (1.2 × 10^{-5} M) with Bu$_3$SnH (2.4 × 10^{-5} M) in the presence of TFA (2.4 × 10^{-5} M) in CH$_2$Cl$_2$ at 25 °C. Dotted line: the spectrum of **2**. Solid line: the spectrum measured 24 h after the addition of Bu$_3$SnH and TFA.

Scheme 2. Reactions of Porphyrinoids with Reducing Reagents



The ^{1}H NMR spectral changes are demonstrated in Figure 2 (and Figure S1). When Bu$_3$SnH and TFA were added to the solution of **2** in CD$_2$Cl$_2$, the peak of the protons on the ethylene bridges (C9−C10 and C19−C20 moieties) at 9.45 ppm disappeared along with the growth of new peaks at 6.15 and 9.47 ppm. The former peak is located in the range observed for typical olefinic protons.[11] The latter peak integrated as four protons is rather broad and exchangeable with D$_2$O, indicative of pyrrole NH protons (Figure 2 inset). A broad peak is observed in a field similar to that seen for

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(6) Vogel, E.; Köcher, M.; Schmickler, H.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 257−259.

(7) (a) Hayashi, T.; Nakashima, Y.; Ito, K.; Ikegami, T.; Aritome, I.; Suzuki, A.; Hisaeda, Y. *Org. Lett.* **2003**, *5*, 2845−2848. (b) Hayashi, T.; Nakashima, Y.; Ito, K.; Ikegami, T.; Aritome, I.; Aoyagi, K.; Ando, T.; Hisaeda, Y. *Inorg. Chem.* **2003**, *42*, 7345−7347.

(8) Vogel, E.; Grigat, I.; Köcher, M.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1655−1657.

(9) Nonell, S.; Borrell, J. I.; Borrós, S.; Colominas, C.; Rey, O.; Rubio, N.; Sánchez-García, D.; Teixidó, J. *Eur. J. Org. Chem.* **2003**, 1635−1640.

(10) Similar spectral changes were also reported for the previous pyrrolophanediene porphycene synthesis. See ref 8.

(11) McMurray, J. *Organic Chemistry*, 3rd ed.; Wadsworth: Belmont, CA, 1992; Chapter 13, pp 442−487.

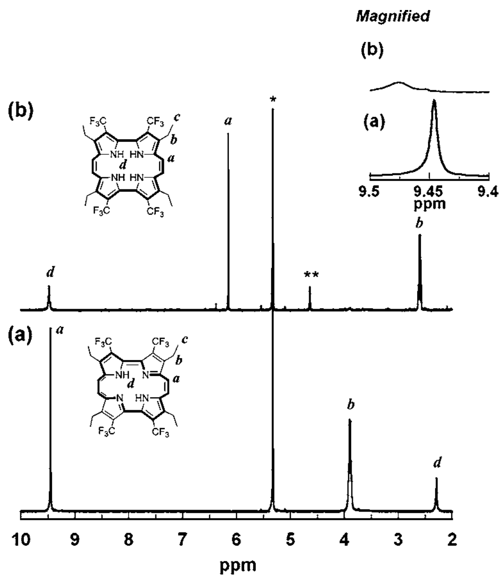

Figure 2. ^{1}H NMR spectra of **2** in the absence and presence of Bu_3SnH/TFA in CD_2Cl_2: (a) in the absence of Bu_3SnH and TFA; (b) 24 h after the addition of Bu_3SnH and TFA. Inset: the magnified spectra at the low field region. The peaks with asterisks (*) and (**) originated from the residual protons of the solvent and excess Bu_3SnH, respectively. The methyl protons in the peripheral ethyl group (peak ***c***) are located out of the range in the figures at 1.63 ppm in the absence of Bu_3SnH/TFA and at 1.17 ppm after the addition of the reducing reagent.

the NH protons of bipyrrole **3**, although the NH protons in **2** are observed at 2.29 ppm due to the ring current effect in the 18π-conjugated system.[7a] The protons in the peripheral ethyl groups are observed in a more upfield region when compared to those in **2**. These spectroscopic characteristics indicate that the product structure coincides with the 20π-conjugated porphycene **1**. The loss of aromaticity in **1** is also indicated in the ^{13}C NMR spectrum (Figure S2). All peaks of the carbons on the pyrrole rings in **1** shifted to a more upfield region when compared with the spectrum for **2** (110−130 ppm for **1**, 110−150 ppm for **2**). The ^{19}F NMR spectrum of the reaction product (Figure S3) shows the peak for the fluorine atom of the CF_3 group at −55.66 ppm, whereas the fluorine atoms in **2** are observed in the downfield region (−51.80 ppm). This finding also supports the nonaromaticity of **1**.[12]

The reaction with Bu_3SnH/TFA or aqueous $Na_2S_2O_4$ was also examined for the etioporphycene without CF_3 groups **6** and the trifluoromethylated etioporphyrin **7** (Scheme 2). However, no UV−vis spectroscopic change was observed for both compounds even upon the addition of the reducing reagents, suggesting that the reactivity of **2** toward the reducing reagents would mainly stem from the positive shift of the reduction potential for **2**: $E_{\mathrm{red}} = -0.14$ V in **2**, −0.92 V in **6**, −0.80 V in **7** (vs Ag/AgCl, in PhCN).[7a]

Compound **1** is expected to be relatively stable toward dioxygen because the parent compound, **2**, has a positively shifted redox potential when compared with that of the porphycene without CF_3 groups, **6**. To confirm this tendency, **1** was prepared by the reduction of **2** with sodium dithionite in THF−water. After being quickly purified by silica gel chromatography under aerobic conditions, **1** was isolated as a yellow powder in 91% yield. The product was dissolved in CH_2Cl_2 in air at 22 °C and then stored in air. Surprisingly, the UV−vis spectrum measured after 24 h indicates that more than 98% of **1** still remained as the 20π-form. Upon the addition of DDQ, **1** was returned to **2** (Figure S7).

We successfully obtained a yellow crystal of **1** with the orthorhombic crystal system from THF−water in the presence of sodium dithionite as **1·(THF)$_2$**, where two THF molecules are contained in one porphycene ring. The molecular structure of **1·(THF)$_2$** determined by X-ray crystallography is shown in Figure 3. Similar to the structure of **2** previously reported,[7a] the porphycene framework of **1·(THF)$_2$** is strongly ruffled and each bipyrrole is twisted due to steric repulsion of the CF_3 groups. The dihedral angle of the two bipyrroles is 50.83°, much larger than that in **2** (23.13°). These structural features result from the loss of aromaticity in **1**. However, the bipyrrole moieties are not significantly twisted as the previously reported pyrrolophane-

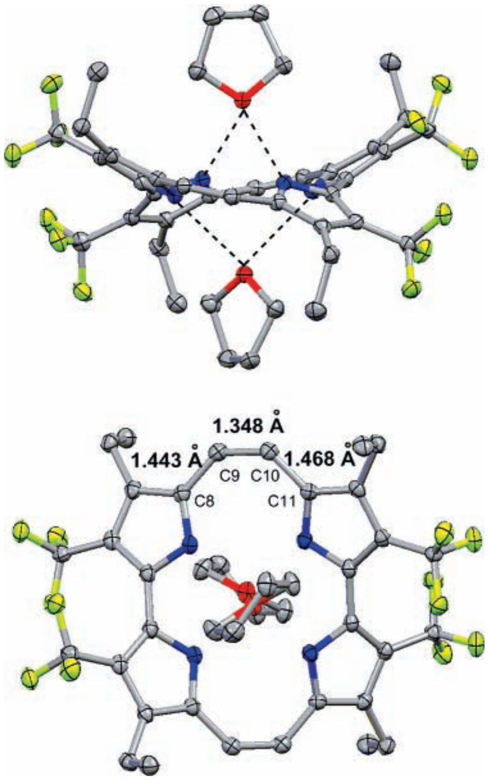

Figure 3. ORTEP drawings of **1·(THF)$_2$** with thermal ellipsoids at 50% probability. Top: perspective view. Bottom: macrocycle view. The dotted lines in the top figure represent the hydrogen bondings.

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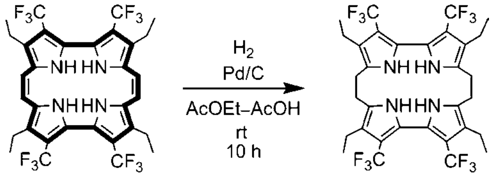
[12] The observation of peaks in the upfield region for ^{1}H and ^{13}C NMR, compared with the parent 18π-conjugated molecule, was also reported in ref 8. However, the tendency of the peak shifts is quite different, probably because of the differences in the orientations of the two bipyrrole moieties.

diene porphycene (64.3°).[8] The bond lengths between C8−C9, C9−C10, and C10−C11 in **1·(THF)$_2$** are 1.443, 1.348, and 1.468 Å, respectively. In the case of **2**, the lengths of the corresponding bonds are 1.407, 1.388, and 1.401 Å, respectively. The bond distance between C9−C10 in **1·(THF)$_2$** is significantly shorter than the other two bonds in this molecule, whereas the distances for the three bonds in **2** are almost similar. This tendency reflects that the ethylene bridge in **1** has a rather olefinic character, as suggested in the ^{1}H NMR spectroscopy. The oxygen atoms of two THF molecules are close to the NH protons with the distance of 2.968 Å of average, suggesting the formation of hydrogen bondings between the oxygen atoms in THF and the pyrrole NHs in the crystal state. The hydrogen bondings are also suggested by the downfield shift of the pyrrole NH proton in the ^{1}H NMR spectrum of **1** containing THF (Figures S4−S6).

The olefinic character of the ethylene bridge in **1** was revealed by the hydrogenation in the presence of Pd/C at room temperature (Scheme 3). The reaction smoothly afforded the hydrogenated compound **8** as determined by NMR (Figures S8−S10) and FAB-MS. The 18π-conjugated porphycene **2** also gave the same product. Probably, **1** is transiently formed during the reaction. In contrast, the non-trifluoromethylated porphycene **6** showed a complicated reaction behavior affording many unidentified products. The trifluoromethylated porphyrin **7** has poor reactivities under the same conditions due to its low solubility.

Scheme 3. Hydrogenation of **1**



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8

The conversion of **2** into **1** is supposed to proceed by the typical 2H$^+$−2e$^-$ transfer mechanism because no reaction was observed upon the addition of only a hydride donor (≡1H$^+$ and 2e$^-$) to **2**. Therefore, the injection of 2H$^+$ and 2e$^-$ by typical 2H$^+$−2e$^-$ donors such as hydroquinones would be possible. When **2** was mixed with trimethylhydroquinone **9** in THF (Scheme 2), the UV−vis spectral changes during the reaction were similar to that observed during the reaction of Bu$_3$SnH/TFA (Figure S11). The half-life time of **2** (1.0×10^{-5} M) in the presence of **9** (1.5×10^{-3} M) was calculated to be 122 s at 25 °C. The reaction rate was found to be dependent on the oxidation potential of the employed hydroquinone because monomethylhydroquinone **10** reacted with **2** more slowly with the same half-life time at the higher concentration of **10** (3.0×10^{-2} M).

In conclusion, we successfully isolated and characterized the stable 20π-conjugated porphycene having trifluoromethyl groups in the periphery of the framework. All the reactions described here were carried out in homogeneous reaction media, whereas the previous preparations of the 20π-conjugated porphyrins have been attained by metal-catalyzed reduction in a heterogeneous system.[3] The availability of the homogeneous reaction system provides us with a good opportunity to discuss the mode of the reaction, including sequential electron and proton transfer, one-step hydrogen atom transfer, or proton-coupled electron transfer (PCET). The investigation of the reaction mechanism during the conversion of the 18π/20π-conjugation system of porphyrinoids, based on their redox potentials and basicities, is now in progress.[13]

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Supporting Information Available: Experimental procedures, NMR and UV−vis spectra, and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) Preliminarily, it was found by the TFA titration experiments that the nitrogen atoms in **2** are less basic than those in **6**, suggesting that the redox potential would be a more significant factor for the conversion into the 20π-form rather than basicity.