

Porphyrin Synthesis in Water Provides New Expanded Porphyrins with Direct Bipyrrole Linkages: Isolation and Characterization of Two Heptaphyrins

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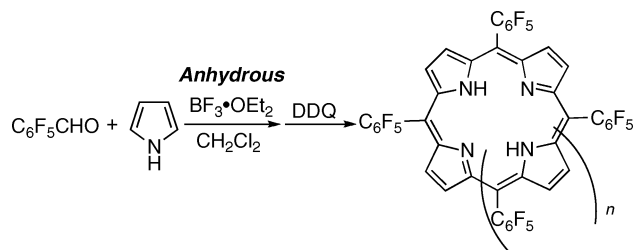
Lindsey's porphyrin synthesis consists of acid-catalyzed condensation between pyrrole and aldehydes, followed by appropriate oxidation.¹ Naturally, the dehydrative condensation in the first step is carried out in anhydrous conditions and is quite unusual to conduct in aqueous media.² However, water often offers new possibilities in organic synthesis because of its unique physical and chemical properties, where rate enhancements and selectivity improvements are realized through enhanced hydrophobic interaction and/or enrichment of organic substrates in specific local environments.³ In light of the recent development of aqueous acid catalysis⁴ and its application to dehydrative esterification reactions,^{4c} we envisaged that the condensation between aldehydes and pyrrole in water would lead to new types of porphyrinoids.⁵

We selected pentafluorobenzaldehyde as the aldehyde for the aqueous porphyrin synthesis, with a hope to find novel expanded porphyrins.⁶ Expanded porphyrins, which are porphyrin analogues with more than four pyrrolic subunits, have attracted increasing attention because of their properties, such as interesting structural features, multiple redox behavior, and unique metal coordination capability. We have already reported that the porphyrin synthesis with C₆F₅CHO as an aldehyde in anhydrous dichloromethane provides a series of expanded porphyrins (Scheme 1).^{6c}

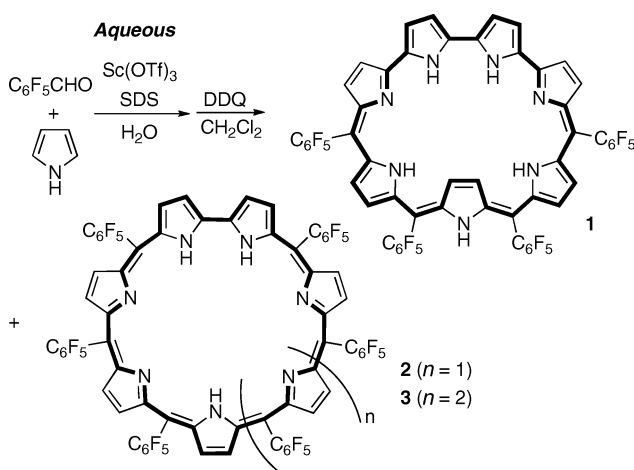
To a vigorously stirred mixture of C₆F₅CHO, pyrrole, and sodium dodecyl sulfate (SDS) in water was added Sc(OTf)₃. The mixture was stirred for 5 h. The reaction mixture was extracted with ethyl acetate and concentrated. The residue was oxidized with DDQ in dichloromethane. Surprisingly, there was trace sign of the formation of porphyrin or expanded porphyrins with an equal number of pyrrole units and bridging methine carbons, which are formed in the anhydrous reaction. Instead, intense peaks at 1169.86 and 1523.08 were detected by MALDI-TOF mass spectroscopy (Supporting Information, SI). Then the mixture was passed through a short alumina column, and greenish solution was eluted with dichloromethane. After this band, a red fraction was eluted with ethyl acetate, from which red–purple porphyrinoid compound **1** was obtained in 5% yield.

On the basis of an ion peak at 1170.1486 by high-resolution electrospray ionization time-of-flight (HR-ESI-TOF) mass spectrum, the formula of **1** was determined to be C₅₆H₁₇F₂₀N₇ (calcd for C₅₆H₁₈F₂₀N₇ = 1170.1455 [(M + H)⁺]). The ¹H and ¹⁹F NMR spectra of **1** in acetone-*d*₆ elucidated its symmetric structure. Importantly, the aromatic nature of **1** is clearly suggested by the significant down- and upfield shifts: 12 β-pyrrolic protons appear at δ = 8–10 ppm and 2 β-pyrrolic protons at δ = 0.33 ppm, indicating that **1** has a rather planar structure with one inverted pyrrole unit (SI). These NMR data suggested **1** to be [30]heptaphyrin(1.1.1.1.0.0.0), which has never been isolated before (Scheme 2).⁷ An addition of trifluoroacetic acid (TFA) to a red solution of **1** gave a blue solution of its protonated form, of which ¹H NMR indicated that two pyrrole units were inverted. UV/vis absorption

Scheme 1



Scheme 2



spectra of **1** and its TFA salt are shown in Figure 1. Finally, X-ray crystallographic analysis of the TFA salt of **1** elucidated its unique structure, which consists of a directly linked tetrapyrrole⁸ unit and a tripyrrodimethene unit (Figure 2).⁹ Reflecting its aromatic character, the framework is nearly planar except for two inverted pyrroles which are slightly tilted from the plane.

The HR-ESI-TOF mass analysis of the first eluted greenish band indicated that it contained a mixture of macrocycles, [30]heptaphyrin(1.1.1.1.1.1.0) (**2**, *n* = 1, *m/z* = 1526.1120) and [34]octaphyrin(1.1.1.1.1.1.0) (**3**, *n* = 2, *m/z* = 1769.1311), each of which has one direct bipyrrole linkage. After separation, we obtained [30]heptaphyrin(1.1.1.1.1.1.0) **2** as a major compound in 5% yield. ¹H NMR spectrum of **2** exhibited 14 pyrrolic β-protons in a normal region, and ¹⁹F NMR revealed the presence of six different C₆F₅ groups (SI). UV/vis absorption spectrum of **2** was intensified significantly upon the addition of excess TFA, indicating planarization of **2** by protonation. Accordingly, ¹H NMR spectrum of **2** in TFA-*d* indicates the aromatic, symmetric nature of protonated **2** with three inverted pyrroles (SI). X-ray crystallographic analysis of protonated **2**, of which single crystals were obtained from a solution of **2** in TFA–CHCl₃, elucidated its flat and symmetric structure (SI).¹⁰ Judging from its unsymmetrical and nonaromatic

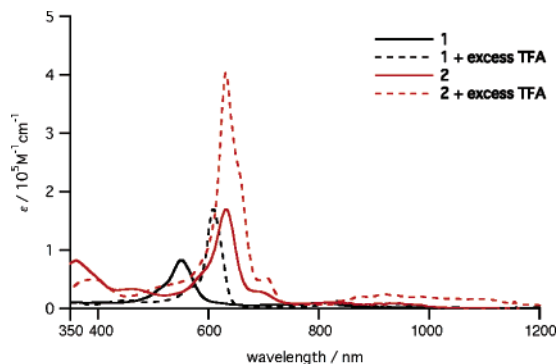


Figure 1. UV/vis absorption spectra of **1**, **2**, and their protonated forms (in acetone for **1** and in CHCl_3 for **2**).

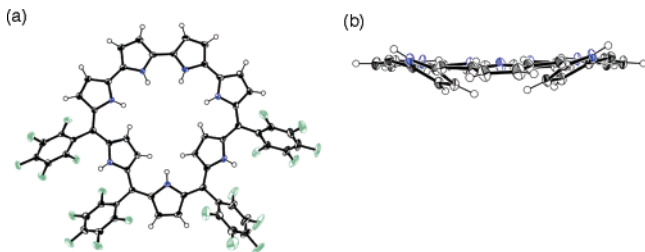
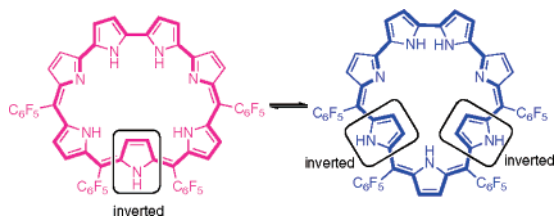


Figure 2. X-ray structure of protonated **1**. Top view (a) and side view (b). Solvent and TFA molecules are omitted for clarity. The thermal ellipsoids are at the 50% probability level.

Scheme 3



character in NMR, heptaphyrin **2** would take a twisted conformation as octaphyrin **3**, of which the structure was confirmed by X-ray analysis (SI).

Interestingly, the color of **1** was heavily dependent on the solvent: red–purple in acetone and ethyl acetate, and blue in MeOH, acetonitrile, CH_2Cl_2 , and CHCl_3 . Since the shape of absorption in the blue solution is similar to that of the TFA salt of **1** (SI), the color change probably stems from flipping behavior of pyrroles (Scheme 3 and SI). Moreover, addition of water to a solution of **1** in acetone also induced color change (Figure 3), for which a water complex $\mathbf{1}\cdot\mathbf{2H}_2\mathbf{O}$ was detected by ESI-TOF mass spectroscopy.

Formation of these unexpected expanded porphyrins is intriguing in view of the mechanism of porphyrinogen formation. ESI-TOF mass analysis of the reaction mixture prior to oxidation showed a marked difference between the aqueous and nonaqueous conditions (SI). The reaction mixture in anhydrous CH_2Cl_2 clearly included cyclic oligopyrroles as expected. In contrast, a series of mass peaks, which can be assigned as linear oligopyrroles, were detected in the aqueous reaction. Such difference in the oligopyrrole formation should lead to these novel expanded porphyrins. In a micelle, the reaction proceeds under highly concentrated conditions, which favors linear oligopyrroles rather than cyclic ones. However, the reaction of $\text{C}_6\text{F}_5\text{CHO}$ with pyrrole under solvent-free conditions

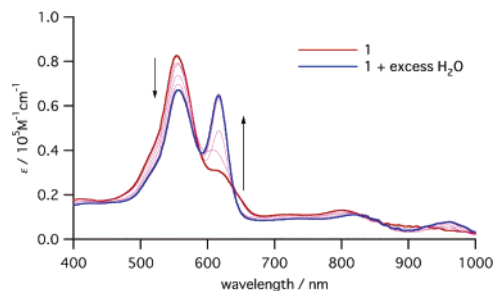


Figure 3. UV/vis absorption spectra of **1** in acetone and in acetone with excess H_2O .

provided only corrole as a porphyrinoid.¹¹ Thus, the observed absence of corrole in our procedure would indicate that preferential formation of longer oligopyrroles is specific to the aqueous micellar system.

In conclusion, $\text{Sc}(\text{OTf})_3$ -catalyzed reaction of $\text{C}_6\text{F}_5\text{CHO}$ and pyrrole in an aqueous micellar system provided expanded porphyrins with direct bipyrrole linkages, of which two novel heptaphyrins have been structurally characterized, thus showing that the aqueous phase offers a new route to novel expanded porphyrins.

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Supporting Information Available: General procedures, spectral data for compounds, and CIF files for **1**, **2**, and **3**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (9) Crystal data for TFA salt of **1**: $\text{C}_{61}\text{H}_{21}\text{F}_{23}\text{N}_7\text{O}_5$, $M_w = 1425.85$, monoclinic, space group $P2_1/c$ (No. 14), $a = 10.3820(18)$ Å, $b = 18.552(3)$ Å, $c = 28.499(5)$ Å, $\beta = 91.956(3)^\circ$, $V = 5485.9(17)$ Å³, $Z = 4$, $D_{\text{calc}} = 1.726$ g/cm³, $T = 90$ K, 77 840 measured reflections, 9664 unique reflections, $R = 0.0916$ ($I > 2.0\sigma(I)$), $R_w = 0.2670$ (all data), GOF = 1.048 ($I > 2.0\sigma(I)$).
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