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MacDonald-Type Reactions Using Bisacrylaldehydes: Synthesis of an Expanded Sapphyrin and Vinylogous Hexaphyrins†

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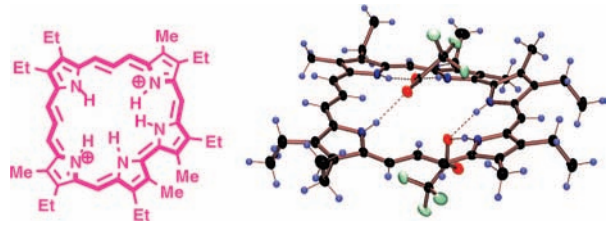
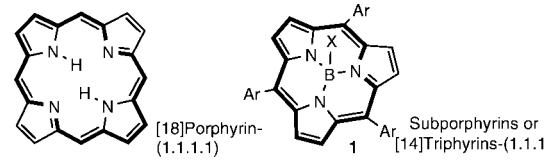
ABSTRACT



Acid-catalyzed condensations between a dipyrrylmethane and a pyrrole bisacrylaldehyde gave an unusual stretched sapphyrin structure together with a hexaphyrin byproduct. A diazulihexaphyrin was prepared similarly. The highly diatropic sapphyrin analogue was isolated as a dication and was characterized by X-ray crystallography.

Porphyrin analogues continue to attract considerable attention,[1−5] in part due to their potential for applications in medicine[6] and in the development of novel optical materials,[7] selective anion recognition systems, and chemical sensors.[8] Furthermore, these systems often generate coordination complexes or organometallic derivatives that can stabilize unusual oxidation states,[3,9] and this can lead to the development of new catalytic systems.[10] Expanded porphyrin structures also show considerable conformational variations[11] and in recent work have been shown to facilitate Möbius aromaticity.[12] Subporphyrins **1**, tripyrrolic porphyrin analogues that are built from three pyrrolic subunits, have also been a recent addition to the porphyrin analogue family and show promise in the development of supramolecular systems.[13] These contracted porphyrins can be considered to be [14]triphyrins-(1.1.1) because the tripyrrolic system is linked by three one-carbon bridges and facilitates 14π electron delocalization pathways as opposed to the 18π electron pathways associated with true porphyrins.



In a recent study,[14] we demonstrated that a pyrrole bisacrylaldehyde **2** could undergo an acid-catalyzed "3 + 1" condensation with a tripyrrane to give an aromatic trapezoidal

† Conjugated Macrocycles Related to the Porphyrins. 50.

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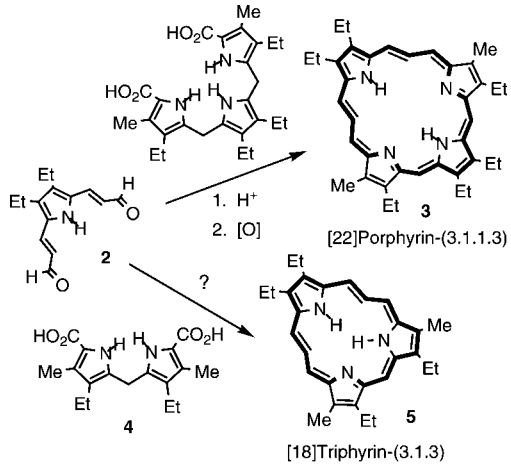
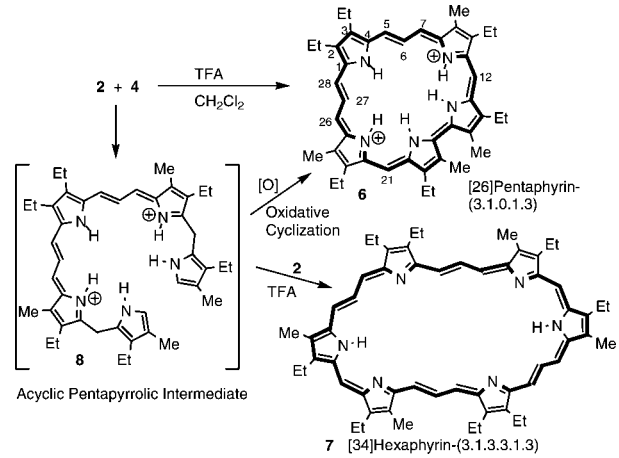
Scheme 1



Scheme 2



porphyrin analogue **3** with 22π electron delocalization pathways (Scheme 1). This expanded system showed highly diatropic characteristics in TFA−$CDCl_3$ and underwent an unusual *EZ* isomerization in the presence of $PdCl_2$ to give a Pd(II) complex.[14] We speculated that dialdehyde **2** might also undergo a "2 + 1" condensation with a dipyrrylmethane **4** to give [18]triphyrin-(3.1.3) **5** (Scheme 1). This system would represent an expanded contracted porphyrin where the tripyrrolic structure regains 18π electron delocalization pathways. These reactions are variations on MacDonald's "2 + 2" method for porphyrin synthesis,[15] but we recognized that condensations of this type do not always give 1:1 adducts.[16] In some cases, 2 equiv of each reactant can be incorporated into a much larger ring system (e.g., figure-eight octaphyrins[16a] and turcasarin[16b]), and the possibility that a conjugated hexapyrrolic expanded porphyrin might be formed as a byproduct or the major product was also considered as a possible outcome.

Dipyrrylmethane **4** was reacted with dialdehyde **2** in a 1:1 ratio in the presence of TFA in dichloromethane for 3 h (Scheme 2).[17] After the compound was washed with water and aqueous TFA, the solvent was removed and the residue chromatographed on grade 3 alumina to give a major reddish-pink fraction, followed by a minor blue fraction. The red fraction was recrystallized from chloroform−hexanes to give a green powder, but spectroscopic analyses were not consistent with the proposed triphyrin **5** or a hexapyrrolic product. This aromatic macrocycle was isolated as the bis-TFA salt of a diprotonated species and was shown to be a pentapyrrolic macrocycle **6** that was constructed from 2 equiv of dipyrrylmethane **4** and 1 equiv of dialdehyde **2**. The proton NMR spectrum unambiguously demonstrated that this product is an expanded sapphyrin[18] system **6** with 26π electron pathways. The minor product, isolated in 6% yield, was identified as the vinylogous hexaphyrin **7**, and no trace of the targeted triphyrin could be identified. The "stretched" pyrrole dialdehyde **2** presumably reacts with 2 equiv of **4** to form an acyclic pentapyrrolic intermediate **8** (Scheme 2). The acyclic oligopyrrole must then undergo a facile oxidative coupling reaction to give the pentaphyrin **6**. On the other hand, the intermediate **8** can also react with another 1 equiv of dialdehyde **2** to give a hexaphyrin **7** with 34π electron delocalization pathways. As the pentaphyrin arises from a 2:1 ratio of reactants, the reaction was repeated with 1 equiv of **2** and 2 equiv of dipyrrylmethane **4**. Using these conditions, the yield of the pentaphyrin was increased to 22%. Although the formation of the pentaphyrin system was unexpected, the oxidative coupling step proposed for macrocycle formation is not unprecedented.[19,20] For instance, Sessler reported a synthesis of sapphyrins where oxidative ring closure is accomplished using DDQ,[19] and other oxidative coupling reactions have been utilized in the synthesis of larger oligopyrrolic macrocycles.[20] Nevertheless, the expanded sapphyrin **6** is generated under very mild oxidation conditions, and no oxidants are used apart from exposure to air. In this respect, the oxidative coupling appears to be unique.

In the proton NMR spectra of **6** in $CDCl_3$, the pentaphyrin system showed a substantial diatropic ring current and two doublets and a singlet were noted in the downfield region at 12.5, 12.4, and 12.2 ppm corresponding to the external bridging methines (Figure 1), while in the upfield region a 2H triplet was found at −8.5 ppm. Impressively, the overall difference

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(17) Usually an oxidation step would be included in a MacDonald-type procedure, but treatment with DDQ or $FeCl_3$ gave inferior results and resulted in substantial decomposition.

(18) Sapphyrins, or [22]pentaphyrins-(1.1.1.1.0), are fully conjugated pentapyrrolic macrocycles with a bipyrrolic component linked to three other pyrroles by single carbon bridges and were first isolated by R. B. Woodward in the mid-1960s. For a review, see ref 8.

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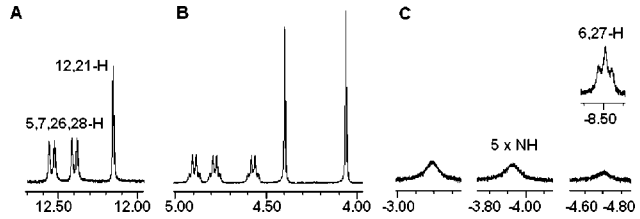


Figure 1. Partial 400 MHz proton NMR spectrum of **6** in $CDCl_3$. (A) Downfield resonances for external bridging protons. (B) Region between 4 and 5 ppm showing abnormally downfield shifted CH_3 and CH_2 units. (C) Upfield region showing three types of NH resonance and a triplet for the internal methine protons.

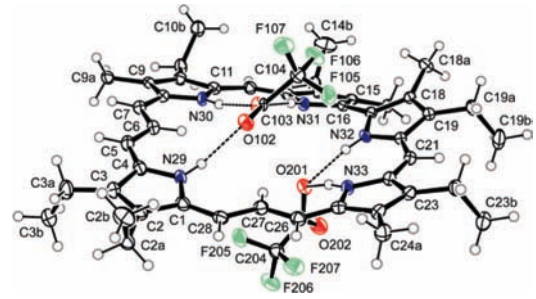


Figure 3. ORTEP-3 drawing (50% probability level, hydrogen atoms drawn arbitrarily small) of pentaphyrin **6**·2TFA.

in chemical shifts ($\Delta\delta$) between the upfield and downfield resonances was >21 ppm. The methyl and CH_2 units of the ethyl groups attached to the pyrrole moieties were also abnormally shifted downfield to between 4 and 5 ppm. The proton and carbon-13 NMR spectra for **6** confirmed the symmetry of the porphyrinoid macrocycle. In addition, three upfield resonances corresponding to a total of five NH protons could be identified in the ^{1}H NMR spectra, supporting the identity of this species as a diprotonated dication. The UV−vis spectrum for **6** in chloroform gave a very strong Soret band at 535 ppm, followed by Q bands at 684, 754, and 840 nm (Figure 2). This result further supports the proposed porphyrin-like aromatic character of **6**, although the expanded chromophore leads to significant bathochromic shifts. Addition of TFA to chloroform solutions of **6** gave rise to virtually no changes in the spectra, but more surprisingly there was also little change in the spectra in the presence of 10% DBU-$CHCl_3$. The pentaphyrin dication is very stable and resists deprotonation to the corresponding free base form, and this result suggests that the free base pentaphyrin is significantly more basic than DBU.

The identity of **6** was confirmed as being the bis-TFA salt by X-ray crystallography (Figure 3). This data also shows that the pentaphyrin is a reasonably planar macrocycle, which is consistent with the strongly aromatic character of the compound, although there are some significant deviations from planarity, particularly the 31.9(1) degree twist for the bipyrrolic unit about C16−C17 which is necessary to accommodate the seven internal hydrogen atoms.[21a] The macrocycle is formally a 26π electron-delocalized system but the bond lengths of the 33 framework atoms suggest that there is a dominant 23 atom delocalization pathway that passes through all five of the nitrogen atoms. In common with other polypyrrolic macrocycles that crystallized in the presence of TFA,[21b−d] **6**·2TFA exhibits strong hydrogen bonding with the counterions with donor hydrogen to acceptor oxygen bond distances ranging from 1.83(3) to 1.98(3) Å. All five pyrrole hydrogen atoms in $\mathbf{6}H_2^{2+}$ are involved in H-bonding, three to one $CF_3CO_2^-$ and two to another.

The proton NMR spectrum of hexaphyrin **7** could only be obtained in the presence of a large excess of TFA but showed even more diatropic character than pentaphyrin **6** (Figure 4). This spectrum corresponds to the tetraprotonated form and for this species the total chemical shifts ranged from −11.25 to 17.30 ppm, a $\Delta\delta$ value of >28.5 ppm. This is one of the largest $\Delta\delta$ values ever reported for a diamagnetic compound, although a [42]porphyrin-(5.5.5.5) gave a $\Delta\delta$ of almost 31.5 ppm.[22] In order to be sufficiently planar for macrocyclic aromaticity, hexaphyrin **7** must adopt the unusual conformation where the three carbon bridges take on two different configurations. In the downfield region, the four types of external methine protons gave rise to a triplet, two overlapping doublets and a singlet at 17.3, 14.8, and 13.8 ppm, respectively. In the upfield region, three singlets corresponding to three different types of internal NH showed up at −6.4, −6.6, and −8.7 ppm, and two doublets and a triplet corresponding to the internal *meso*-protons resonated at −10.6, −10.8, and −11.2 ppm. The UV−vis spectra for the hexaphyrin **7** were also very inform-

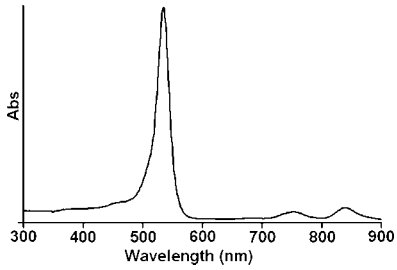


Figure 2. UV−vis absorption spectra for **6** in $CHCl_3$.

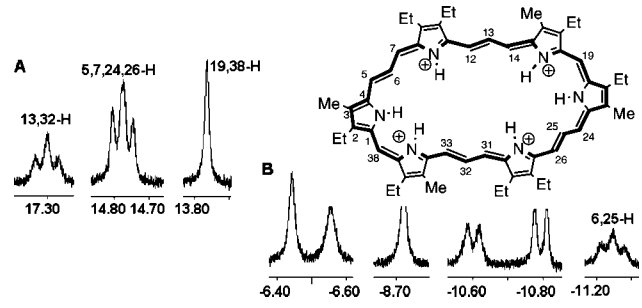
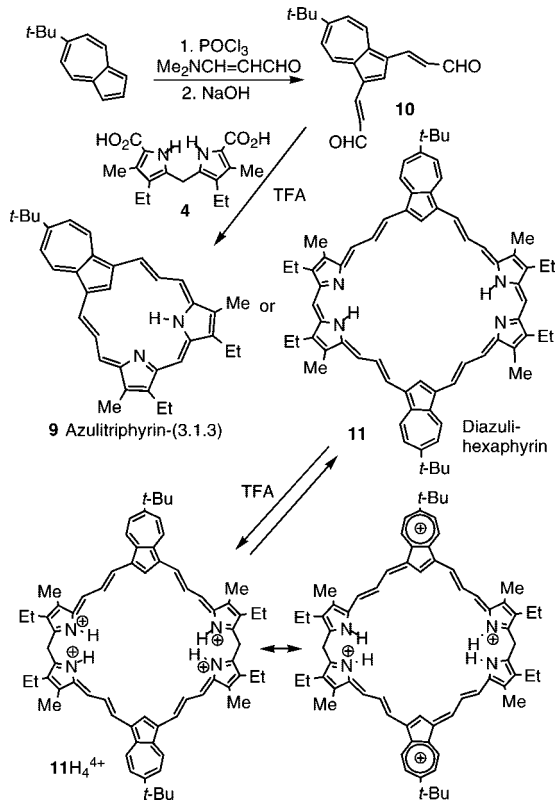


Figure 4. Partial 400 MHz proton NMR spectrum of hexaphyrin $\mathbf{7}H_4^{4+}$ in TFA−$CDCl_3$ showing details of the downfield (A) and upfield (B) regions.

Scheme 3



ative. In 5% Et_3N-$CHCl_3$ solution, two weak bands were found at 452 and 626 nm and in chloroform solution, slightly stronger bands showed up at 463 and 647 nm. However, in 5% TFA−$CHCl_3$ solution a strong split absorption band appeared at 645 and 670 nm with a weak band located at 461 nm. These data suggest that the hexaphyrin system only behaves like an aromatic porphyrinoid under highly acidic conditions. The tetracation must favor a fairly planar conformation, but less protonated species and the free base appear to be nonplanar and therefore nonaromatic compounds.

The same synthetic strategy was used in an attempt to prepare azulitriphyrin-(3.1.3) **9**. 6-*tert*-Butylazulene[23] was reacted in refluxing 1,2-dichloroethane with $POCl_3$ and 3-dimethylaminoacrylaldehyde (vinylogous Vilsmeier−Haack reaction) to give the related bis-acrylaldehyde **10** (Scheme 3). This was condensed with dipyrrylmethane **4** in the presence of TFA in dichloromethane under nitrogen for 30 min. After being washed with water and acidified with TFA, the evaporated residue was purified on a flash silica column eluting with 10% MeOH−$CHCl_3$ to give a dark greenish powder. Precipitation from acetone with hexanes gave the product as a dark solid in 64% yield. This compound was extremely insoluble in chloroform and pyridine and did not give interpretable spectral data in CD_3OD, CD_3CN, or acetone-d_6. However, addition of several drops of TFA into the NMR tube with $CDCl_3$ greatly improved the solubility and generated a deep bluish solution. In the proton NMR spectrum, the downfield region showed a singlet at 12.6 ppm corresponding to the NHs. A singlet, a doublet, a multiplet and a doublet showed up at 9.1, 8.7, 8.2, and 7.7 ppm, respectively, corresponding to the internal CHs, the four protons on the azulene moiety and the *meso*-protons. The singlet at 4.6 ppm indicates that the compound undergoes protonation on the *meso*-position between two pyrrole subunits under these conditions. Based on the proton NMR data, two possible structures could be formulated, a contracted azulitriphyrin **9** or an expanded diazulihexaphyrin **11** (Scheme 3).[24] Initial ESI MS data seemed to indicate that **9** had been formed ($C_{35}H_{39}N_2^+$; *m*/*z* 487), but field desorption mass spectrometry demonstrated that the compound was the expanded diazulihexaphyrin **11** ($C_{70}H_{77}N_4^+$; *m*/*z* 973). In both the ESI and FD MS spectra, significant peaks were noted at *m*/*z* 486 and 487, but these were shown to be due to a double charged species. The UV−vis spectra of **11** were also informative. In 5% Et_3N−chloroform, two weak bands were found at 426 and 606 nm, and in chloroform solution, two bands were located at 435 and 589 nm. However, in 5% TFA−chloroform a very different spectrum was obtained showing a strong absorption band at 698 nm and two other bands at 339 and 499 nm. These data indicate that diazulihexaphyrin **11** behaves like a totally different chromophore under strongly acidic conditions compared to neutral and basic conditions, which is consistent with the NMR data and is due to C-protonation interrupting conjugation in the macrocycle (Scheme 3).

In conclusion, attempts to carry out "2 + 1" condensations between bis-acrylaldehydes and a dipyrrylmethane did not afford triphyrins but instead gave novel expanded porphyrin structures. The expanded sapphyrin structure **6** gave a porphyrin-like UV−vis spectrum and was fully characterized by X-ray crystallography. Both the expanded sapphyrin and a hexaphyrin byproduct **7** showed highly diatropic characteristics for the fully protonated species by proton NMR spectroscopy, where the $\Delta\delta$ value for the hexaphyrin was >28 ppm. An azulene bis-acrylaldehyde also reacted with dipyrrylmethane **4** to give a diazulihexaphyrin **11** but this system did not favor macrocyclic aromaticity. The new expanded porphyrins all have large cavities that may give them useful anion binding characteristics.[8] In addition, the long wavelength absorptions exhibited by **6** and **7** could make these expanded porphyrins suitable candidates for use as photosensitizers in photodynamic therapy.[25]

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Supporting Information Available: Experimental procedures, selected UV−vis, ^1H NMR and ^{13}C NMR spectra, and crystallographic data for **6** are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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