

**[48]Dodecaphyrin-(1.0.1.0.1.0.1.0.1.0) and
[64]Hexadecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0):
The Largest Cyclopolypyrroles**

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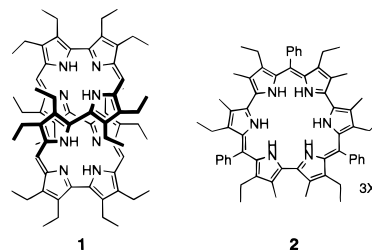
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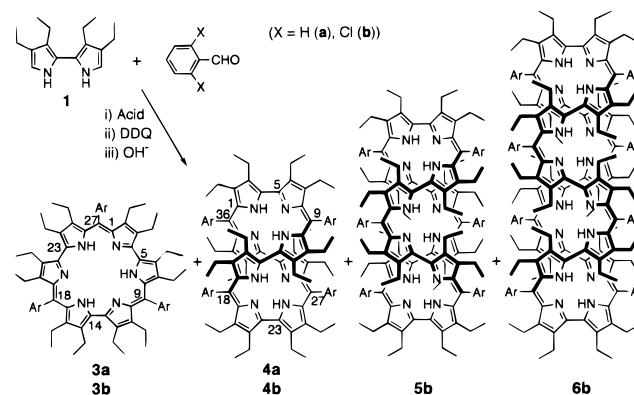
Expanded porphyrins containing more than four pyrrole units have been drawing great attention from the viewpoints of both theoretical aspects and biomedical applications.¹ Pentapyrrolic sapphyrin² and pentaphyrin,³ and hexapyrrolic rosarin,⁴ rubyrin,⁵ and hexaphyrin⁶ are well documented so far. Higher homologues, [32]octaphyrin-(1.0.1.0.1.0.1.0)⁷ and [40]decaphyrin-(0.0.1.0.1.0.0.1.0.1.0),⁸ are macrocycles containing eight and ten pyrroles and are of great interest because of their figure-eight conformation and anion binding properties.⁹ [32]Octaphyrin-(1.0.1.0.1.0.1.0) **1** was prepared by an acid-catalyzed MacDonald-type¹⁰ [2+2+2+2] condensation of 5,5'-diformyl-2,2'-bipyrrole with 2,2'-bipyrrole or by an analogous [4+4] condensation of tetrapyrrole derivatives in yields of 7–11% (Scheme 1).^{7a,7b} Whereas these reactions are designed not to give macrocycles with an odd number of 2,2'-bipyrrole units, it was shown that condensation of 2,2'-bipyrrole with aldehydes analogous to the Rothmund porphyrin synthesis¹¹ resulted in the cyclization of three bipyrrole units and three aldehyde molecules to give tricationic rosarin **2** exclusively in a 70% yield.⁴ This high yield condensation using simple starting materials is attractive as a synthetic method for higher homologues of expanded porphyrins that have never been reported. We describe here our finding that [32]octaphyrin-(1.0.1.0.1.0.1.0), [48]dodecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0), and [64]hexadecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0) are formed by this Rothmund-type synthesis if 2,2'-bipyrrole and aldehyde with bulky substituents are condensed under weakly acidic conditions especially in the presence of zinc acetate.

3,3',4,4'-Tetraethyl-2,2'-bipyrrole (0.2 mmol) and benzaldehyde (0.2 mmol) were allowed to react in the presence of 0.25 equiv of trifluoroacetic acid (TFA) in CH₂Cl₂ (20 mL) at room

Scheme 1



Scheme 2



temperature for 24 h according to the synthetic procedure of **2** from 3,3'-dimethyl-4,4'-diethyl-2,2'-bipyrrole and benzaldehyde,⁴ which is similar to the synthesis of *meso*-tetraaryloctaethylporphyrins.¹² After oxidation of the condensation products with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), deprotonation with 10% aqueous NaOH solution, and chromatographic separation, an orange compound **3a** and a purple compound **4a** were afforded in 60% and 7% yield, respectively (Scheme 2). The ¹H NMR and FABMS spectra of **3a** and **4a** are consistent with 2,3,6,7,11,12,15,16,20,21,24,25-dodecaethyl-9,18,27-triphenylrosarin and 2,3,6,7,11,12,15,16,20,21,24,25,29,30,33,34-hexadecaethyl-9,18,27,36-tetraphenyl[32]octaphyrin-(1.0.1.0.1.0.1.0), respectively. The X-ray crystallographic analysis of **2** indicates that the π -conjugated system is highly deviated from a planar structure to relieve steric constraints between peripheral substituents.⁴ Therefore, the presence of more bulky substituents at the pyrrole β -positions in **3a** than in **2** would cause greater deformation of the π -conjugated system out of planarity. This explains the blue shift by 62 nm of the UV-vis absorption maximum of the tricationic rosarin (**3a**·3H)³⁺3Cl⁻ at 490 nm in comparison with that of **2** at 552 nm.⁴ On the other hand, the UV-vis absorption band of **4a** at 569 nm is red-shifted from that (548 nm) of 2,3,6,7,11,12,15,16,20,21,24,25,29,30,33,34-hexadecaethyl[32]octaphyrin-(1.0.1.0.1.0.1.0) **1**. This red shift is ascribed to the electronic effect of tetraphenyl substituents at the methine positions of **4a** but not to their steric effect. Therefore, the stereochemical features of the π -conjugated system of **4a** and **1** should be similar. As is seen from the X-ray structure of **1**,^{7a} the figure-eight conformation of octaphyrin would provide enough space to accommodate phenyl groups at the methine positions.

The above relationship between the structure and electronic spectrum predicts that the increase in steric hindrance between peripheral substituents leads to octaphyrin formation over rosarin formation. This is actually the case when 2,6-dichlorobenzaldehyde was allowed to react under the same reaction conditions as

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above, giving rosarin **3b**, octaphyrin **4b**, and a blue compound **5b** in 17%, 19%, and 5% yield, respectively (Scheme 2).¹³ Although the yields of these products simply decreased in a 1:1 mixture of AcOH/CH₂Cl₂ instead of cat.TFA/CH₂Cl₂, addition of Zn(OAc)₂·2H₂O (2 equiv) resulted in the formation of a new blue compound **6b** in a 9% yield along with **3b** (5%), **4b** (11%), and **5b** (6%).¹⁴ Introduction of the chlorine atoms caused a slight red shift (5 nm) in the UV-vis spectra of **3b** (478 nm) and **4b** (574 nm) in comparison with **3a** and **4a**, respectively. The much longer wavelengths of the absorption bands of **5b** (648 nm) and **6b** (678 nm) than that of **4b** are indicative of higher homologues of expanded porphyrin. The TOFMS spectra of **5b** (*m/z* = 2395.1) and **6b** (*m/z* = 3193.7) are in good agreement with the theory for [48]dodecaphyrin-(1.0.1.0.1.0.1.0.1.0) (2396.20) with six bipyrrrole units and for [64]hexadecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0) (3194.93) with eight bipyrrrole units, respectively. The most salient feature in the single-crystal X-ray structure of **5b** is the fact that a zigzag-tracked π -conjugation plane is folded to form a wall of a pipe with a tetragonal cut end of 9.9 (width) \times 5.2 (depth) Å (see Figure 1).¹⁵ While the π - π stacking between the front side and the backside of the figure-eight conformation of the reported octaphyrins and decaphyrin results in van der Waals contact (\sim 3 Å separation) leaving no space between,^{7,8} the corresponding separation in the crystal structure of **5b** is \sim 5 Å. Introduction of bulkiness at the 3,3'-position of the bipyrrrole is crucial for the formation of octaphyrin, dodecaphyrin, and hexadecaphyrin because it causes a twist of the bipyrrrole unit and makes the formation of rosarin unfavorable. The bulky aryl groups help increase the steric crowding at the bipyrrrole 3,3'-diethyl groups by way of the direct influence on the 4,4'-diethyl groups. In fact, large N-C(α -pyrrole)-C(α -pyrrole)-N torsion angles (174°, 44°, and -133°) in the bipyrrrole units are observed for **5b**, while the dipyrromethene units (pyrrole-C(Ar)=pyrrole) are mostly coplanar and the 2,6-dichlorophenyl groups are almost perpendicular to them.

Since there was observed a tendency that the yields of **3b** and **4b** increased and that of **5b** decreased with time in the cat.TFA/CH₂Cl₂ system, a cyclic hexamer of bipyrrrolylmethane should be converted into thermodynamically more stable trimeric and tetrameric macrocycles, owing to acid-catalyzed fragmentation and recyclization.¹⁶ This process should be retarded by using AcOH as a weaker acid than TFA.¹⁷ When a d₄-acetic acid solution of 3,3',4,4'-tetraethyl-2,2'-bipyrrrole, 2,6-dichlorobenzaldehyde, and Zn(OAc)₂·2H₂O in the same concentrations as those for the preparation experiment was monitored by ¹H NMR, the starting materials disappeared in 15 min at 20 °C. Thus, linear bipyrrrolylmethane oligomers should be rapidly equilibrated and those with six and eight bipyrrrole units are expected to exist as one of the major components under the present concentrations (0.01 M) of the reactants.¹⁸ The effect of Zn(OAc)₂·2H₂O is

(13) The TOFMS analysis showed formation of decaphyrin (obs, 1999.0; theory for the average mass, 1996.83).

(14) The TOFMS analysis showed formation of decaphyrin and tetradecaphyrin (obs, 2798.6; theory for the average mass, 2795.6).

(15) Recrystallization of **5b** from CH₂Cl₂/acetone gave crystals of 1:2 composition of **5b** and CH₃COCH₃. Crystal data for **5b**·(C₃H₆O)₂: C₁₄₄H₁₅₀N₁₂O₂Cl₁₂, *M* = 2512.33, monoclinic, space group *P*₂/*n* (no. 14), *a* = 16.037(5), *b* = 24.020(6), *c* = 17.810(3) Å, β = 94.74(2)°, *V* = 6837(3) Å³, *Z* = 2, *D*_{calc} = 1.220 g/cm³, μ (Mo K α) = 2.98 cm⁻¹, *T* = 299 K, crystal size 0.40 \times 0.30 \times 0.20 mm. A total of 13177 unique reflections were collected (4 < 2 θ < 55°) on a Rigaku AFC5R diffractometer using graphite-monochromated Mo K α radiation. The standard reflections showed no decay over the course of data collection; 3916 reflections with *I* > 2.00 σ (*I*) were used for structure solution and refinement. The structure was solved by the direct method (SIR92) and refined by the full-matrix least-squares method (Texsan). All nonhydrogen atoms were refined anisotropically. Hydrogen atoms were included at standard positions (C-H = 0.95 Å) but not refined. The refinement converged at *R* = 0.087, *R*_w = 0.062, and GOF = 2.10.

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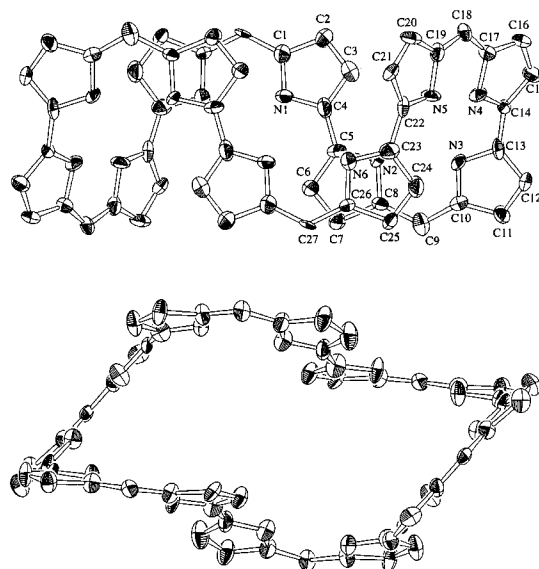


Figure 1. ORTEP drawings of **5b** showing 50% probability thermal ellipsoids and atom-numbering scheme. Twenty four ethyl groups (at C2, C3, C6, C7, C11, C12, C15, C16, C20, C21, C24, C25, C2*, C3*, C6*, C7*, C11*, C12*, C15*, C16*, C20*, C21*, C24*, C25*), six 2,6-dichlorophenyl groups (at C9, C18, C27, C9*, C18*, C27*), and acetone solvates are omitted for clarity. A side view (top) and a top view (bottom) are shown. Selected distances (Å) and angles (deg): N1–C1, 1.38(1); N1–C4, 1.34(1); C1–C2, 1.41(1); C2–C3, 1.37(1); C3–C4, 1.43(1); C4–C5, 1.46(1); C1–N1–C4, 110(1); C5–N2–C8, 105.9(9); C10–N3–C13, 111(1); C14–N4–C17, 108.4(9); C19–N5–C22, 109.1(9); C23–N6–C26, 106(1); C8–C9–C10, 123(1); C17–C18–C19, 125(1); C1–C27–C26, 126(1); N1–C4–C5–N2, 174(1); N2–C8–C9–C10, 13(2); N3–C10–C9–C8, 7(2); N3–C13–C14–N4, 44(1); N4–C17–C18–C19, 10(2); N5–C19–C18–C17, 1(2); N5–C22–C23–N6, -133(1); N6–C26–C27–C1, 8(2); N1–C1–C27–C26, -3(2).

remarkable in the formation of the giant macrocycle with eight bipyrrrole units, and it seems to play a key role in the cyclization process of these bipyrrrolylmethane oligomers.

[40]Decaphyrin-(0.0.1.0.1.0.0.1.0.1) prepared by the condensation of tripyrrrole with bipyrrrole dialdehyde was named as turcasarin, and it has been known as the largest expanded porphyrin since 1994.⁸ It is of great importance that cyclopoly-pyrroles with a larger ring size are obtainable by a simple methodology and that they have a large cavity surrounded by a wall of zigzag-tracked π -conjugation system. A molecular model of **6b** on the basis of the X-ray structure of **5b** suggests a cylindrical cavity with a diameter of \sim 10 Å. The inclusion phenomenon of these expanded porphyrins is of great interest and is now under study.

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Supporting Information Available: Experimental procedures, characterization data for **3a**, **4a**, and **3b–6b**, and listings of the details in the structure determination for **5b**, including crystallographic data, atomic coordinates, thermal parameters, bond lengths, bond angles, torsion angles, least-squares planes, and ORTEP drawings. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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