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Bis(azafulvene) as a Versatile Building Block for Giant Cyclopolypyrroles: X-ray Crystal Structure of [64]Hexadecaphyrin(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0)

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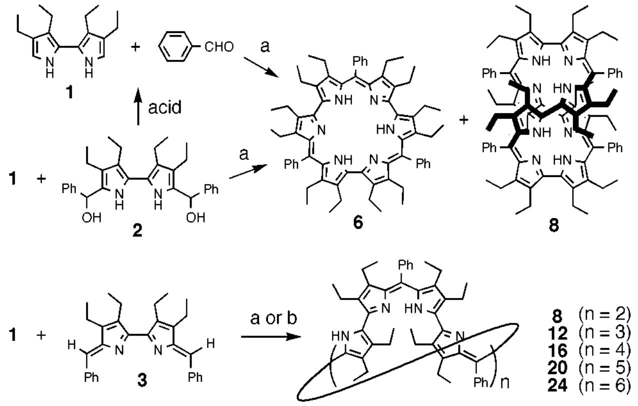
The figure-eight structure of [40]decaphyrin(1.0.1.0.0.1.0.1.0.0) indicated that fully conjugated porphyrinoids need not be topographically flat.[1] We have recently proceeded one step further to demonstrate that giant porphyrinoids with 12- and 16-pyrrole units have a cylindrical cavity.[2] The promise of these giant porphyrinoids for use in molecular recognition and catalysis accelerates study on the synthetic methodology.[3] Acid-catalyzed MacDonald-type condensation has been one of the most important methods and afforded [32]octaphyrin(1.0.1.0.1.0.1.0) and [40]-decaphyrin(1.0.1.0.0.1.0.1.0.0).[1,4] Very recently [32]octaphyrin (1.0.0.0.1.0.0.0) has been formed by oxidative ring closure of linear oligopyrroles with α-free pyrrolic units at both ends.[5] On the other hand, condensation of α-free pyrrole derivatives with aldehydes analogous to the Rothemund porphyrin synthesis gave [24]hexaphyrin(1.0.1.0.1.0) known as rosarin,[6] [26]hexaphyrin(1.1.1.1.1.1),[7] [32]octaphyrin(1.0.1.0.1.0.1.0),[2] [48]-dodecaphyrin(1.0.1.0.1.0.1.0.1.0.1.0),[2] and [64]hexadecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0).[2] Although the Rothemund-type reaction of 2,2′-bipyrrole does afford cyclopolypyrroles with world-record ring sizes, the chromatographic separation of a mixture of bipyrrole-based homologues is not easy. Thus, this work is intended to explore a facile synthetic method for even larger cyclopolypyrroles by using modified MacDonald-type reactions which would give a mixture of tetrapyrrole-based homologues.

The condensation reaction of 3,3′,4,4′-tetraethyl-2,2′-bipyrrole (**1**, 0.2 mmol) and 5,5′-bis(phenylhydroxymethyl)-3,3′,4,4′-tetraethyl-2,2′-bipyrrole (**2**, 0.2 mmol) was carried out for 1 h in a solvent mixture of AcOH (2.5 mL) and CH_2Cl_2 (2.5 mL) containing 2 equiv of $Zn(OAc)_2 \cdot 2H_2O$. Oxidative workup with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave a mixture of 2,3,6,7,11,12,15,16,20,21,24,25-dodecaethyl-9,18,27-triphenylrosarin (**6**)[2] 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) (**8**)[2] in 11 and 14% yield, respectively. When the reaction was run for 24 h, **6** and **8** were produced in 24 and 20% yield, respectively. The formation of **6** as a major product indicates that tetrapyrrole-based cyclooligomers should be decomposed and recyclized to bipyrrole-based cyclooligomers under the acidic reaction conditions. This reaction was further complicated by the acid-catalyzed decomposition of **2** to benzaldehyde and **1**. ^1H NMR monitoring indicated that **2** (0.02 mmol) did not react with **1** (0.02 mmol) in $CDCl_3$ (0.5 mL) in 3 h when 5% decomposition of **2** to give benzaldehyde has occurred. Addition of CD_3CO_2D (2 μL) not only triggered the condensation reaction between **1** and **2** but also enhanced decomposition of **2** to give benzaldehyde in 20% yield in 30 min. Therefore, the MacDonald-type condensation of **1** and **2** should be accompanied by the Rothemund-type condensation of **1** and benzaldehyde under the above reaction conditions. Since water is responsible for acid-catalyzed redistribution among cyclooligomers of different ring size before DDQ oxidation, a new bipyrrole building block which eliminates undesired formation of water should be preferred. Addition of phenyllithium (5 equiv) to 5,5′-diformyl-3,3′,4,4′-tetraethyl-2,2′-bipyrrole in THF would generate the tetraanion that was quenched with water to give 95% yield of **2**. When the tetraanion was quenched with acetic anhydride (5 equiv) instead of water, a yellow compound **3** was obtained in 55% yield. The ^{13}C NMR signal due to the methine carbon connecting pyrrole and phenyl group indicates change in hybridization from sp^3 in **2** (68.2 ppm) to sp^2 in **3** (131.5 ppm). The resonances due to the pyrrole ring carbons undergo great downfield shifts from 120.4, 122.5, 122.8, and 128.0 ppm in **2** to 168.8, 141.7, 147.6, and 154.8 ppm in **3**. These data are consistent with the bis(azafulvene) structure of **3**. The ROESY spectrum of **3** demonstrated trans stereochemistry of the phenyl groups with respect to the pyrrole-β-ethyl groups.[8] The polar electronic structure characteristic of fulvene in **3** would induce facile electrophilic addition to **1** without the undesired equilibria caused by water.

Scheme 1



a) 1) $Zn(OAc)_2 \cdot 2H_2O$/ AcOH-CH_2Cl_2, 2) DDQ; b) 1) no catalyst / CH_2Cl_2, 2) DDQ.

When a mixture of **1** and **3** is reacted in the AcOH− CH_2Cl_2−$Zn(OAc)_2 \cdot 2H_2O$ system for 1 h, **8** was obtained in 20% yield with no trace of **6**. In addition to **8**, blue fractions showing UV−vis maxima at 674, 674, 708, and 728 nm were obtained in 6, 7, 4, and 3% yield, respectively, by chromatographic separation using silica gel and polydivinylbenzene gel. The ESI-TOF MS data of these four fractions (*m*/*z* 1982.2708, 2643.6856, 3304.1440, and 3965.5523 for monocations) are in good agreement with the theory for [48]dodecaphyrin(1.0.1.0.1.0.1.0.1.0.1.0) (**12**, M + 1 = 1982.2603), [64]hexadecaphyrin(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0)

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(8) A cross-peak was observed between the methylene protons at 2.65 ppm and the methine proton at 6.98 ppm in the ROESY spectrum.

10.1021/ja005588o CCC: $19.00

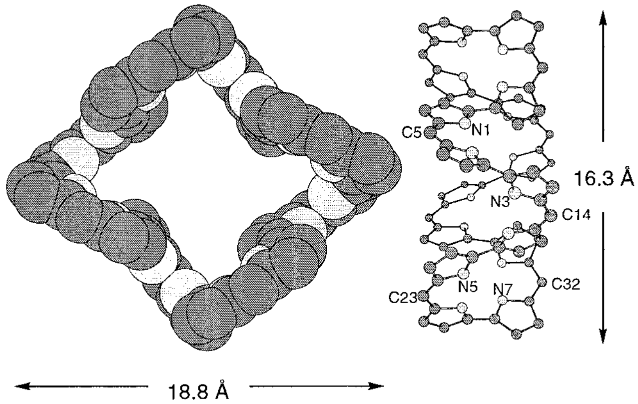

Figure 1. X-ray structure of **16** with its atom-numbering scheme. Thirty-two ethyl groups at the pyrrole-β positions and eight phenyl groups at the *meso* positions are omitted for clarity. A front view of a space filling model (left) and a side view of a ball-and-stick model (right) are shown. Selected distances (Å) and angles (deg): N1−C1, 1.337(6); N1−C4, 1.383(5); C1−C2, 1.403(6); C2−C3, 1.385(6); C3−C4, 1.443(7); C4−C5, 1.401(6); C5−C6, 1.398(6); N2−C6, 1.402(5); N2−C9, 1.329(5); C6−C7, 1.436(6); C7−C8, 1.378(6); C8−C9, 1.424(6); C1−N1−C4, 110.2(4); C6−N2−C9, 107.6(4); C4−C5−C6, 124.3(4); N1−C4−C5−C6, 8.5(7); C4−C5−C6 N2, 7.8(7); N2−C9−C10−N3, 52.6(6); N4−C18−C19−N5, 171.0(4); N6−C27−C28−N7, 93.4(5); N8−C36−C1*−N1*, 145.0(4).

(**16**, $M + 2 = 2643.6826$), [80]icosaphyrin(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0) (**20**, $M + 2 = 3304.1023$), and [96]tetracosaphyrin(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0) (**24**, $M + 3 = 3965.5212$), respectively. While MS signals associated with higher homologues were detected in the first fraction of GPC,[9] those with an odd number of bipyrrole units have never been detected. This indicates that acid-catalyzed redistribution of cyclooligomers is not taking place under the present reaction conditions. Bis(azafulvene) **3** is so reactive that addition to **1** took place without catalyst in CH_2Cl_2 in 1 h to give **8**, **12**, **16**, **20**, and **24** in 23, 3, 4, 3, and 2% yield, respectively.

The X-ray crystallography of **16** shows the square pillar structure with a tetragonal cut end of 18.8 × 16.3 Å (see Figure 1).[10] The height (14.4 Å) of the pillar corresponds to the *b*-axis of the unit cell. The molecules are stacked precisely face to face to make a channel along the *b*-axis in the crystal packing. The molecule has a C_2 axis of symmetry and large $N-C_{(\alpha-\text{pyrrole})}-C_{(\alpha-\text{pyrrole})}-N$ torsion angles (52.5°, 171.0°, 93.4°, and 145.0°) in the bipyrrole units are observed, while the dipyrrylmethene units (pyrrole−C(Ph)═pyrrole) are mostly coplanar and the phenyl groups are almost perpendicular to them.

Very recently some reports have appeared on the giant porphyrinoids which contain eight to twelve pyrroles and/or related heterocycles.[11] Compared with these, the tetracosaphyrin **24** is a remarkably large compound and its cavity with a diameter more than 20 Å exceeds the molecular size of γ-cyclodextrin itself (ca. 17 Å). It is of great importance that the reaction between 2,2′-diaza-3,3′-bifulvene and 2,2′-bipyrrole provides a series of cyclopolypyrroles with ring sizes varied by a tetrapyrrole unit with the *meso*-phenyl group. Special *meso*-aryl groups such as pentafluorophenyl and 2,6-dichlorophenyl are not necessary. The high reactivity of bis(azafulvene) and the elimination of water-driven equilibria are the key features in our synthesis of giant porphyrinoids. Furthermore, it is promising that bis(azafulvene) has wide application as a powerful building block in porphyrinoid chemistry.[12]

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Supporting Information Available: Experimental details on the synthesis and characterization of compounds **2**, **3**, **12**, **16**, **20**, and **24**, as well as tables of crystallographic data, atomic coordinates, bond lengths, bond angles, thermal parameters, and ORTEP drawings of X-ray structure for **16** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] The observed MS signals at *m/z* 4623, 5283, 5944, and 6604 are associated with 28-, 32-, 36-, and 40-phyrins, respectively.

[10] Recrystallization from benzene/acetone gave crystals of **16**. Crystal data: $C_{184}H_{208}N_{16}$, $M = 2643.66$, monoclinic, space group $C2/c$, $a = 34.611(3)$ Å, $b = 14.3764(14)$ Å, $c = 34.408(4)$ Å, $\beta = 94.085(2)°$, $V = 17077(3)$ Å^3, $Z = 4$, $D_{\text{calc}} = 1.028$ g/cm^3, μ(Mo Kα) = 0.060 mm^{-1}, $T = 299$ K, crystal size 0.30 × 0.30 × 0.30 mm^3. A total of 17212 unique reflections were collected ($2 < 2\theta < 55°$) using graphite-monochromated Mo Kα radiation. $R1 = 0.097$, $wR2 = 0.244$ for 5816 reflections with $I > 2.00\sigma(I)$; $R1 = 0.245$, $wR2 = 0.329$ for all data. GOF (on F^2) = 0.928.

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