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Improved Synthesis of *meso*-Aryl-Substituted [26]Hexaphyrins

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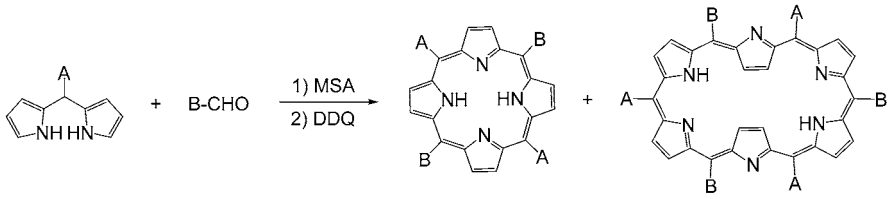
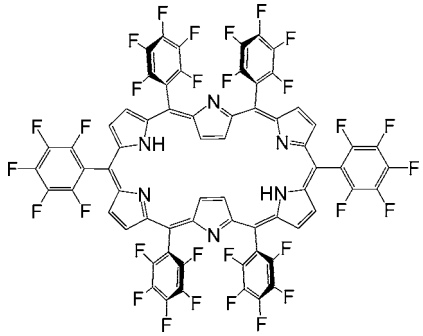
ABSTRACT



Acid-catalyzed reactions of 5-(2′,3′,4′,5′,6′-pentafluorophenyl)dipyrromethane with aryl aldehydes and of 5-(aryl)dipyrromethanes with 2,3,4,5,6-pentafluorobenzaldehyde allowed the preparation of a variety of *meso*-aryl [26]hexaphyrins.

Expanded porphyrins have recently emerged as an intriguing class of functional molecules in light of their interesting optical, electrochemical, and coordination properties.[1,2] Among these, *meso*-aryl-substituted [26]hexaphyrins such as **4a** (Chart 1) can be regarded as real homologues of porphyrin in terms of the conjugated cyclic π-system with alternate arrangement of pyrroles and methine carbon atoms.[3,4] In 1999, Cavaleiro et al. reported the formation of [26]-hexaphyrin **4a** during a Rothemund-type synthesis of *meso*-tetrakis(2,3,4,5,6-pentafluorophenyl)porphyrin.[3] In the mean-

Chart 1. Structure of [26]Hexaphyrin **4a**



time, we reported the synthesis of a series of *meso*-aryl-substituted expanded porphyrins by the modified Rothemund−Lindsey reaction of pyrrole with 2,6-disubstituted electron-deficient aryl aldehydes.[4] A 10-fold increase in the reactant concentrations from 6.7 mM that was optimized for the preparation of porphyrin[5] to 67 mM provided a range of *meso*-aryl-expanded porphyrins including **4a** as a main product (16−20% yield).[4a] [26]Hexaphyrin **4a** is an attractive

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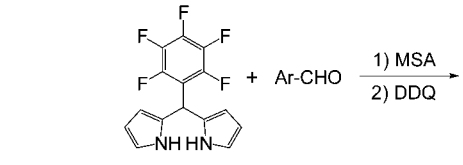
molecule in view of the relatively high yield, the intense absorption band in the visible region, and pronounced aromaticity that arise from the formal 26-π circuit, and the unique rectangular conformation consisting of the two inverted side pyrroles with the nitrogen atoms pointing outward and the four corner pyrroles with the nitrogen atoms pointing inward.[3]

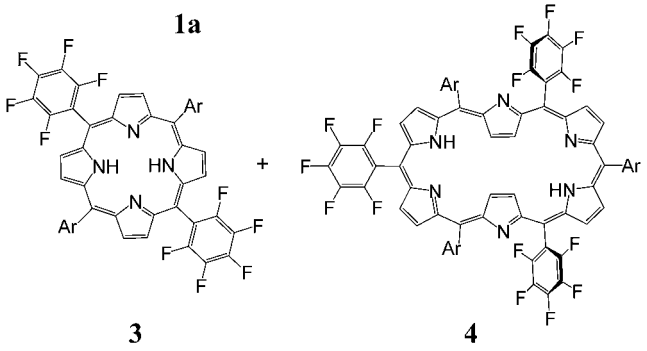
In the Rothemund−Lindsey-type synthesis of 5,10,15,20-tetraarylporphyrins, almost all aromatic aldehydes can be used to provide a range of functional porphyrins with the exception of severely sterically hindered aromatic aldehydes.[5,6] In contrast, the synthetic scope of [26]hexaphyrins was so far limited to the reactions of pyrrole with 2,3,4,5,6-pentafluorobenzaldehyde (**2a**), 2,6-difluorobenzaldehyde, 2,4,6-trifluorobenzaldehyde, and 2,6-dichlorobenzaldehyde, while it failed with benzaldehyde, 2-fluorobenzaldehyde, 2-chlorobenzaldhyde, 2-bromobenzaldehye, and 2,4-difluorobenzaldehyde.[4a] This limitation, although not fully understood, suggests the importance of steric congestion around the formyl group as well as the electron-deficient nature of aryl substituents for the formation of *meso*-aryl-expanded porphyrins. Chemical modification of [26]hexaphyrins is somehow possible through the nucleophilic substitution reactions at the *meso*-pentafluorophenyl substituents,[7] but the direct introduction of various aryl groups into hexaphyrin would be a more attractive synthetic approach to functionalized derivatives. In this paper, we report the improved synthesis of [26]hexaphyrins on the basis of the acid-catalyzed reaction of 5-aryl dipyrromethanes and aryl aldehydes. X-ray crystal structures of 5,15,25-tris(2′,6′-dimethoxyphenyl)-10,20,30-tris(2′,3′,4′,5′,6′-pentafluorophenyl)-[26]hexaphyrin **4h** and 5,15,25-tris(anthr-9′-yl)-10,20,30-tris-(2′,3′,4′,5′,6′-pentafluorophenyl)[26]hexaphyrin **4o** are also reported as the first examples of [26]hexaphyrin bearing different *meso*-aryl substituents.[8]

In accord with the previous results,[4a,5] the Rothemund−Lindsey reaction of pyrrole and 2,6-dimethoxybenzaldehyde followed by oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave only porphyrin (7% yield) without the formation of [26]hexaphyrin. On the other hand, the reaction of 5-(2′,3′,4′,5′,6′-pentafluorophenyl)dipyrromethane (**1a**) and 2,6-dimethoxybenzaldehyde (33 mM each in CH_2Cl_2, methanesulfonic acid (MSA) 2 mM, 0 °C, 2 h) followed by oxidation with DDQ (147 mM, room temperature, 5 h) gave porphyrin **3h** (8%) and [26]hexaphyrin **4h** (9%) (Table 1, entry 7). The structure of **4h** was determined by spectroscopic measurements (^{1}H NMR, FAB-MS, and UV−vis) and X-ray crystallography (discussed later). In the ^{1}H NMR spectrum of **4h**, the inner NH protons appear as two broad peaks at −2.43 and −2.25 ppm (−1.98 ppm for **4a**), the inner pyrrolic CH-protons appear as two sharp doublets at −2.79 and −2.73 ppm (−2.43 ppm for **4a**), and the outer pyrrolic CH protons appear as four sharp doublets at 8.85, 9.10, 9.29, and 9.47 ppm (9.11 and 9.44 ppm for **4a**), indicating the slightly enhanced aromaticity and lower molecular symmetry compared with **4a**. Results with other aromatic aldehydes are summarized in Table 1. While the formation of porphyrins was only detected in the reaction of **1a** with sterically unhindered aromatic aldehydes (entries 1, 3, 6, and 12), [26]hexaphyrins and/or octaphyrins were obtained from the reaction of *ortho*-substituted aromatic aldehydes (entries 2, 5, 8, 9, 10, and 11). Further, the reaction of **1a** with 2-nitrobenzaldhyde led to formation of [26]hexaphyrin **4n** (11%), [32]octaphyrin **5n** (14%) and decaphyrin **6n** (5%) (entry 13), suggesting favorable feature of an electron-deficient aryl aldehyde for the formation of higher expanded porphyrins. However, [26]hexaphyrins were not obtained from severely

Table 1. Synthesis of [26]Hexaphyrins



1a



3 **4**

entry	Ar	products: porphyrin	products: hexaphyrin
1	phenyl	**3b** (2%)	**4b** (0%)
2[a]	2-methylphenyl	**3c** (5%)	**4c** (23%)
3	4-methylphenyl	**3d** (10%)	**4d** (0%)
4	2,4,6-trimethylphenyl	**3e** (<1−2%)	**4e** (0%)
5	2-methoxyphenyl	**3f** (4%)	**4f** (14%)
6	4-methoxyphenyl	**3g** (10%)	**4g** (0%)
7	2,6-dimethoxyphenyl	**3h** (8%)	**4h** (9%)
8	2,6-diethoxyphenyl	**3i** (2%)	**4i** (11%)
9	2,6-dibenzyloxyphenyl	**3j** (5%)	**4j** (12%)
10	2,4,6-trimethoxyphenyl	**3k** (6%)	**4k**(12%)
11[a]	naphth-1-yl	**3l** (5%)	**4l**(19%)
12	naphth-2-yl	**3m** (7%)	**4m** (0%)
13[b]	2-nitrophenyl	**3n** (2%)	**4n** (11%)
14	anthr-9-yl	**3o** (0%)	**4o** (0%)
15[c]	phenyl	**3b** (3%)	**4b** (6%)
16[c]	4-methylphenyl	**3d** (9%)	**4d** (11%)
17[c]	4-methoxyphenyl	**3g** (5%)	**4g** (10%)
18[c]	2-naphthyl	**3m** (6%)	**4m** (9%)

[a] Corresponding octaphyrin was formed in a trace amount. [b] Octaphyrin **5n** (14%) and decaphyrin **6n** (5%) were also obtained. [c] The oxidation time with DDQ was 5−10 min.

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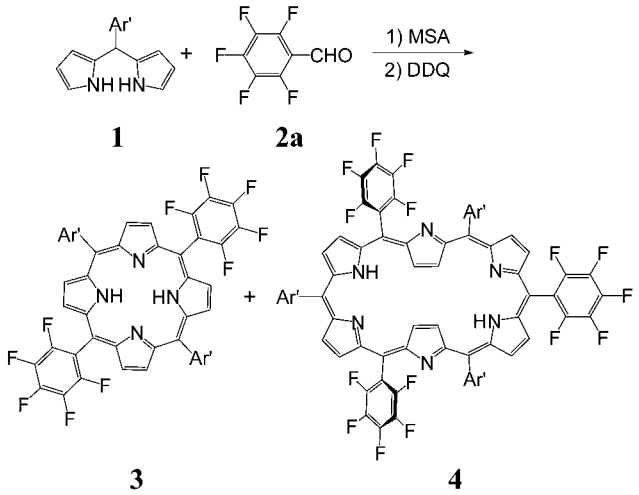
(8) Recently, the reaction of 5-(9-anthryl)dipyrrylmethane with triisopropylsilyl propynal was reported to give [28]hexaphyrin bearing different substituents at the *meso*-positions. Krivokapic, A.; Anderson, H. L. *Org. Biomol. Chem.* **2003**, DOI 10.1039/b306725b.

Scheme 1



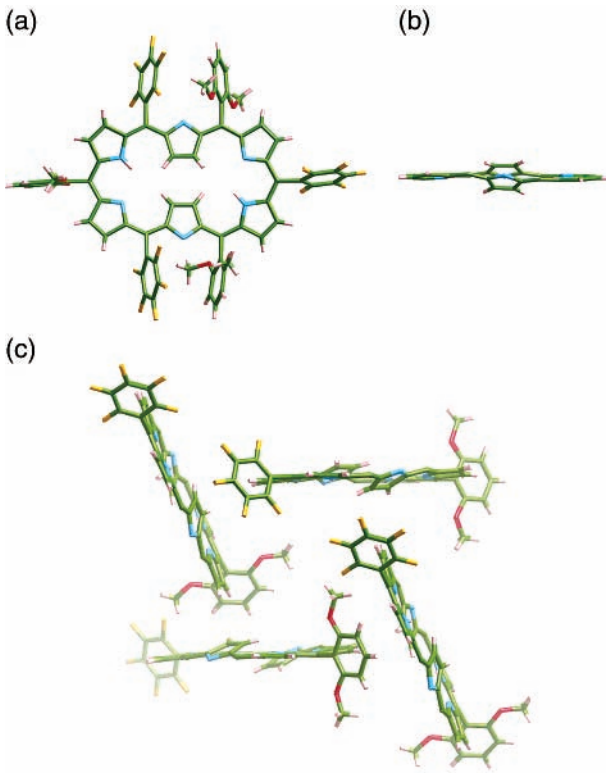


Figure 1. X-ray structures of **4h**: (a) top view, (b) side view, and (c) crystal-packing structure. All *meso*-aryl groups in (b) and some *meso*-aryl groups in (c) are omitted for clarity.

hindered aryl aldehydes such as 2,4,6-trimethylbenzaldehyde and 9-formylanthracene (entries 4 and 14).

Next, we examined the reactions of **2a** with 5-(aryl)dipyrromethane (Scheme 1). In this synthesis, the sterically hindered aromatic aldehydes (2,4,6-trimethylbenzaldehyde and 9-formylanthracene) were converted, by following the method of Lee and Lindsey,[9] into the corresponding dipyrromethanes **1b** and **1c**, respectively, which were then reacted

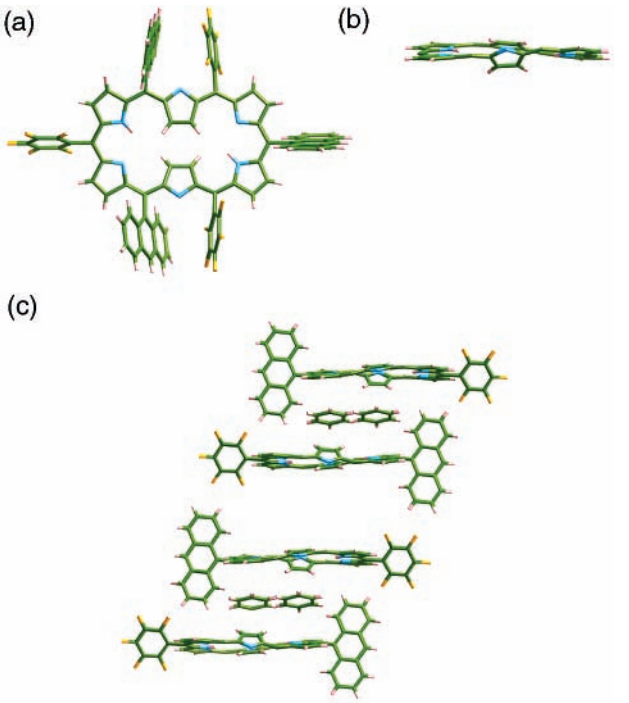


Figure 2. X-ray structures of **4o**: (a) top view, (b) side view, and (c) crystal-packing structure. All *meso*-aryl groups in (b) and some *meso*-aryl groups in (c) are omitted for clarity. Benzene molecules are come from the crystallization solvent.

with **2a** under similar conditions. These reactions gave the corresponding porphyrin **3e** (12%) and [26]hexaphyrin **4e** (15%), and porphyrin **3o** (6%) and [26]hexaphyrin **4o** (10%), respectively. The yields of **3o** and **4o** seem remarkable considering the reported very low yields of *meso*-tetrakis(anthr-9-yl)porphyrin under the Rothemund−Lindsey conditions.[10] When this reaction was applied for 2-nitrobenzaldehyde, the corresponding [26]hexaphyrin **4n** was obtained as a main product (29%) along with the corresponding porphyrin **3n** (2%), octaphyrin **5n** (5%), and decaphyrin **6n** (4%).

In addition, we found that [26]hexaphyrins bearing sterically unhindered *meso*-aryl groups can be prepared by the reaction of **1a** with corresponding aryl aldehyde, by shortening the reaction time with DDQ to only 5−10 min (entries 15−18). [26]Hexaphyrins including **4b**, **4d**, **4g**, and **4m** were slowly decomposed upon treatment with DDQ and almost disappeared after 5 h. Therefore, the absence of [26]-hexaphyrin product in entries 1, 3, 6, and 12 may be ascribed, *not to failure of their formation, but subsequent irreversible reaction with DDQ*. In contrast, [26]hexaphyrins that bear only 2-substituted or 2,6-disubstituted aryl groups are stable upon the treatment with DDQ for longer time, thus suggesting that the above irreversible degradation may be initiated by an oxidative attack of DDQ at the sterically unhindered *meso*-positions of [26]hexaphyrins.

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(10) (a) Cense, J.-M.; Quan, R.-M. *Tetrehedron Lett.* **1979**, *20*, 3725−3728. (b) Banfi, S.; Montanari, F.; Penso, M.; Sosnovskikh, V.; Vigano, P. *Gazz. Chim. Ital.* **1987**, *117*, 689−693.

The X-ray crystal structures of **4h** and **4o** both exhibit a rectangular shape without significant bond-length alternation along the conjugated macrocyclic 26π-network, sharing the characteristic aromatic features reported for **4a** (Figures 1 and 2).[11,12] The mean plane deviations are 0.155 and 0.268 Å for **4h** and **4o**, being slightly smaller than that (0.536 Å) in **4a**.[3] The inverted pyrroles are slightly tilted to the opposite directions, above and below with respect to the macrocyclic plane, giving rise to lower molecular symmetry (C_2). In the solid state, four **4h** molecules form a skewed rhomboid shape, while two **4o** molecules are packed in a head-to-tail parallel manner with the interplanar distance of ca. 7.2 Å. Interestingly, two benzene molecules are found just between two **4o** molecules to complement aromatic π-stacking.

In summary, the acid-catalyzed reactions of either *meso*-(2,3,4,5,6-pentafluorophenyl)dipyrromethane with aryl aldehydes or of *meso*-(aryl)dipyrromethane with 2,3,4,5,6-pentafluorobenzaldehyde allowed the preparation of [26]hexaphyrins with a range of *meso*-aryl substituents including the electron-rich 2,6-dimethoxyphenyl group, sterically unhindered aryl groups, and bulky 2,4,6-trimethylphenyl and 9-anthryl groups. Stable conformations of [26]hexaphyrins are nearly the same, regardless of the electron-rich aryl substituent or sterically demanding 9-anthryl substituent. All the [26]hexaphyrins reported are thermally stable, but those bearing sterically unhindered *meso*-aryl groups are susceptible to oxidative degradation upon the treatment with DDQ. Results presented here suggests that the synthetic scope of *meso*-aryl-substituted [26]hexaphyrins may be wider than previously thought and we are trying to explore a newer synthetic method that will further increase the accessibility of [26]hexaphyrins.

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(11) Selected data for **4h**: ^{1}H NMR (600 MHz, $CDCl_3$) δ −2.79 (d, J = 4.0 Hz, 2H, inner βCH), −2.73 (d, J = 4.2 Hz, 2H, inner βCH), −2.43 (br, 1H, inner NH), −2.24 (br, 1H, inner NH), 3.51 (s, 12H, methoxy), 3.64 (s, 6H, methoxy), 7.10−7.12 (6H, phenyl), 7.80−7.90 (3H, phenyl), 8.95 (d, J = 4.7 Hz, 2H, outer βCH), 9.10 (d, J = 4.7 Hz, 2H, outer βCH), 9.29 (d, J = 4.7 Hz, 2H, outer βCH), 9.47 (d, J = 4.7 Hz, 2H, outer βCH); UV/vis(CH_2Cl_2) $\lambda_{max}(\epsilon)$ 568 (210 000), 717 (23 000), and 1033 (14 000) nm; FAB-MS m/z (rel intensity) 1373.3 (100) [M^+]. Crystal data of **4h**: $C_{72}H_{43}F_{15}N_6O_6$ = 1373, orthorhombic, space group P_{bca} (No. 61), a = 25.50(2) Å, b = 17.27(1) Å, c = 32.08(2) Å, V = 14124(2) Å^3, Z = 8, D_{calcd} 1.494 g/cm^3, T = −150 °C, R = 0.052, R_w = 0.058, GOF = 0.516.

(12) Selected data for **4o**: ^{1}H NMR (600 MHz, $CDCl_3$) δ −2.36 (d, J = 4.0 Hz, 2H, inner βCH), −2.15 (d, J = 4.7 Hz, 2H, inner βCH), −1.91 (br, 1H, inner NH), −1.56 (br, 1H, inner NH), 6.97−7.52 (18H, anthryl), 8.31−8.39 (6H, anthryl), 8.43 (d, J = 4.7 Hz, 2H, outer βCH), 8.86 (d, J = 4.7 Hz, 2H, outer βCH), 8.95 (d, J = 4.7 Hz, 2H, outer βCH), 9.00 (d, J = 4.7 Hz, 2H, outer βCH), 8.98−9.02 (3H, anthryl); UV/vis(CH_2Cl_2) $\lambda_{max}(\epsilon)$ 350 (28 000), 367 (31 000), 389 (32 000), 573 (190 000), 723 (27 000), and 1035 (14 000) nm; FAB-MS m/z (rel intensity) 1493.0 (100) [M^+]. Crystal data of **4o**: $C_{90}H_{41}F_{15}N_6$ = 1493, triclinic, space group P-1 (No. 2), a = 15.722(7) Å, b = 17.056(4) Å, c = 17.622(7) Å, α = 79.99°, β = 64.28°, γ = 72.74°, V = 4059(2) Å^3, Z = 2, D_{calcd} 1.362 g/cm^3, T = −150 °C, R = 0.085, R_w = 0.115, GOF = 2.200. Crystals were grown from a solution of benzene and octane.