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Regioselective nucleophilic substitution reaction of *meso*-hexakis(pentafluorophenyl) substituted [26]hexaphyrin

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Abstract—Reaction of various alkoxides led to the selective replacement of the *p*-fluorine substituents of *meso*-hexakis(pentafluorophenyl) substituted [26]hexaphyrin. Reaction with isopropyl amine gave *meso*-hexakis(4-isopropylamino-2,3,5,6-tetrafluorophenyl) substituted [28]hexaphyrin.

In recent years, expanded porphyrins having a macrocycle larger than porphyrins have emerged as a novel class of functional molecules in light of their fascinating optical, electrochemical, and coordination properties.[1,2] As a simple yet effective protocol, we have reported the modified Rothemund–Lindsey reaction[3] of 2,6-disubstituted electron-deficient arylaldehyde and pyrrole that provides a series of *meso*-aryl substituted expanded porphyrins as real homologues of porphyrin in terms of fully conjugated cyclic π-systems as well as alternate arrangement of pyrroles and methine carbons.[4] Among these, *meso*-hexakis(pentafluorophenyl) substituted [26]hexaphyrin (**1**) that was first reported by Cavaleiro[5] and is the major product formed as much as in ca. 20% yield in our method[4b] is interesting in view of the strong aromaticity arising from 26-π electrons and a unique rectangular shape with two inverted pyrroles with the nitrogen pointing outward. In addition, its sharp Soret-like band is observed at 568 nm in CH_2Cl_2, which may be pertinent to use as a Digital Video Disk (DVD) recording dye, and its lowest excited state is lying rather low at around 1.18 eV, encouraging its uses in far IR absorption pigments or photodynamic therapy. In these applications, it would be very important to fabricate a [26]hexaphyrin chromophore so as to make it soluble in a wide range of solvents depending on the respective uses; quite nonpolar solvents like hexane for spin coating, normal alcohols for dyes, and water for many biological applications including photodynamic therapy. With these in background, we examined nucleophilic substitution reactions at the *p*-fluorine atoms in the *meso*-pentafluorophenyl substituents in **1**, since the analogous reactions have been demonstrated in tetrakis-*meso*-(pentafluorophenyl) substituted porphyrins.[6]

As shown in Scheme 1 and Table 1, refluxing a THF solution of **1** in the presence of excess amounts of alcohols and KOH gave rise to formation of substitution products **2a–g** in moderate to good yields. The substitution regioselectivity was always quite high only at the *p*-fluorine of all the six *meso*-pentafluorophenyl groups. Similar aromatic substitution reaction was also effected by sodium ethoxide (entry 2). The substitution product **2d** is substantially soluble (3×10^{-3} M) in hexane and **2e** shows ca. threefold (1×10^{-2} M) solubility, while **2f** and **2g** exhibit much larger solubility. All these [26]hexaphyrins have essentially the same optical properties as that of **1**. These highly soluble properties in nonpolar solvents are quite important for the spin coating fabrication in DVD and other devices. On the other hand, treatment of **2d** with an excess amount of BBr_3 in CH_2Cl_2 led to formation of **2h** (R = H) that is fairly soluble both in slightly basic aqueous solution and methanol.

In the next step, reaction of **1** with isopropylamine in DMF under refluxing conditions resulted in formation of hexakis(4-isopropylamino-2,3,5,6-tetrafluorophenyl)[28]hexaphyrin (**3**) in 32% yield.[7] This reaction did not need an additional base. A change in π-electronic system was suggested from its absorption spectrum (λ_{max} = 610, 775, 856, and 1035 nm, Fig. 1) that was substantially altered from that of **1** but was

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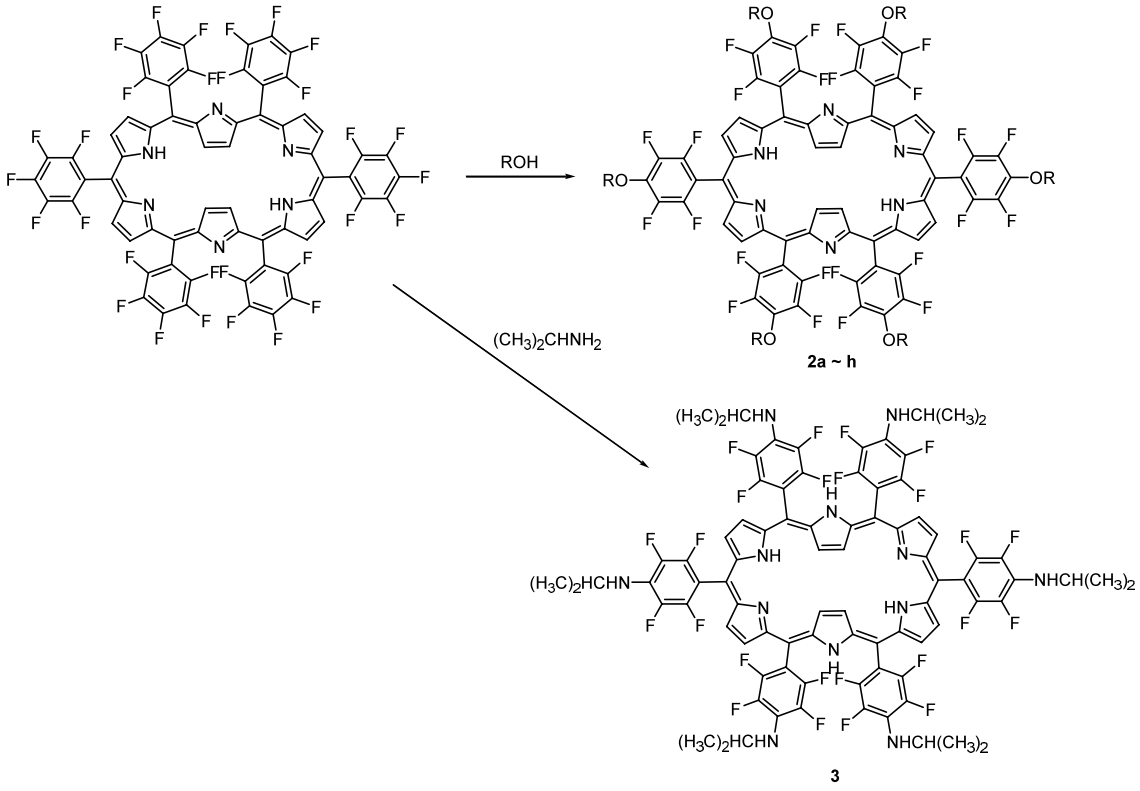

Scheme 1.

Table 1. Syntheses of *p*-substituted hexaphyrins

Entry	Nucleophiles	Conditions	Products	Yield (%)
1	$C_2F_5(CH_2)_3OH$	KOH, THF, Ar, reflux, overnight	**2a** ($R=(CH_2)_3C_2F_5$)	86
2	C_2H_5ONa	EtOH, Ar, reflux, overnight	**2b** ($R=C_2H_5$)	46
3	$CH_3(C_2H_4O)_3OH$	KOH, THF, reflux, overnight	**2c** ($R=(C_2H_4O)_3CH_3$)	32
4	$C_4H_9CH(C_2H_5)CH_2OH$	KOH, THF, reflux, overnight	**2d** ($R=CH_2CH(C_2H_5)C_4H_9$)	75
5	$C_6H_{13}CH(C_4H_9)CH_2OH$	KOH, THF, reflux, overnight	**2e** ($R=CH_2CH(C_4H_9)C_6H_{13}$)	29
6	$CH_3(CH_2)_{15}OH$	KOH, THF, reflux, overnight	**2f** ($R=(CH_2)_{15}CH_3$)	82
7	$C_{10}H_{21}CH(C_8H_{17})CH_2OH$	KOH, THF, reflux, overnight	**2g** ($R=CH_2CH(C_8H_{17})C_{10}H_{21}$)	61
8	$(CH_3)_2CHNH_2$	DMF, Ar, reflux, overnight	**3**	32

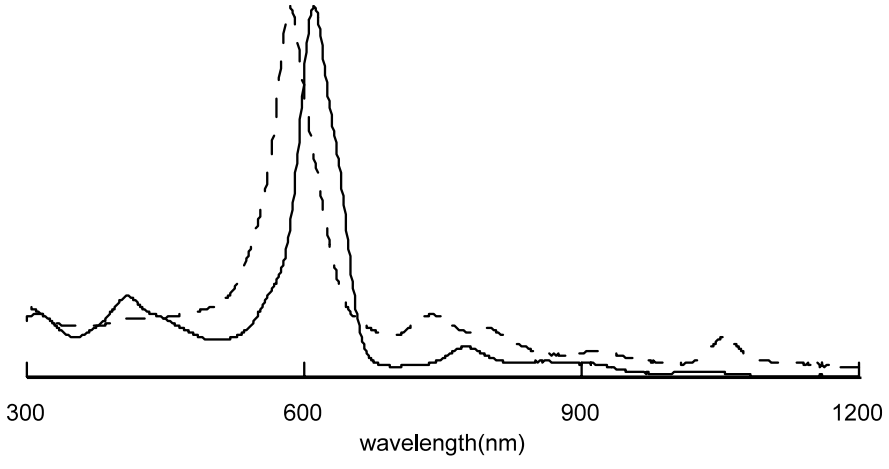

Figure 1. Absorption spectra of **3** (solid line) and its oxidized form (dotted line) in CH_2Cl_2.

similar to that of [28]hexaphyrin.[5] Similar reduction was also effected refluxing a DMF solution of **2b** in the presence of isopropylamine, indicating that the amine can act as a reductant toward [26]hexaphyrin. The X-ray crystal structure of **3** has been determined for the first time for [28]hexaphyrin, which reveals not only a rectangular shape that is nearly the same as that of [26]hexaphyrin,[5] but also the presence of two imino-type pyrroles at the corner positions as well as four amino-type pyrroles at both the corner and middle positions (Fig. 2). The four corner pyrrole rings rest in a roughly planar arrangement, while the middle two pyrrole rings are tilted by ca. 13.2° from the mean plane constituted by the four corner pyrroles. As originally reported by Cavaleiro,[5] the aromatic character of [26]hexaphyrin is evident from its ^{1}H NMR chemical shifts. The inner N–H and β C–H protons appear at high-field region at ca. –2.0 and –2.4 ppm, respectively, and the outer β C–H protons appear at 9.10 and 9.42 ppm. The absorption spectrum displaying a strong and sharp Soret-like band and distinct Q-band-like bands is also indicative of its aromatic character. This aromatic character can be accounted for in terms of the circuit consisting of 26π electrons as indicated by bold line in Scheme 1. On the other hand, much weaker or no aromatic character is expected for a reduced form of hexaphyrin, [28]hexaphyrin, as judged from the number of π-electrons in the circuit and the related properties of larger expanded porphyrins.[4] Nevertheless the ^{1}H NMR spectrum of [28]hexaphyrin **3** reveals rather high-field shifted peaks due to the inner N–H (3.38 ppm) and β C–H protons (1.97 ppm) and low-field shifted peaks due to the outer N–H (7.71 ppm) and β C–H protons (7.83 and 7.93 ppm), possibly indicating its partial aromatic character. In addition, its absorption spectral features exhibiting a relatively sharp Soret-like band and several Q-band-like absorption bands are also suggesting some aromatic character for **3**. Treatment of **3** with DDQ gave rise to formation of its oxidized form of [26]hexaphyrin as indicated the spectral changes

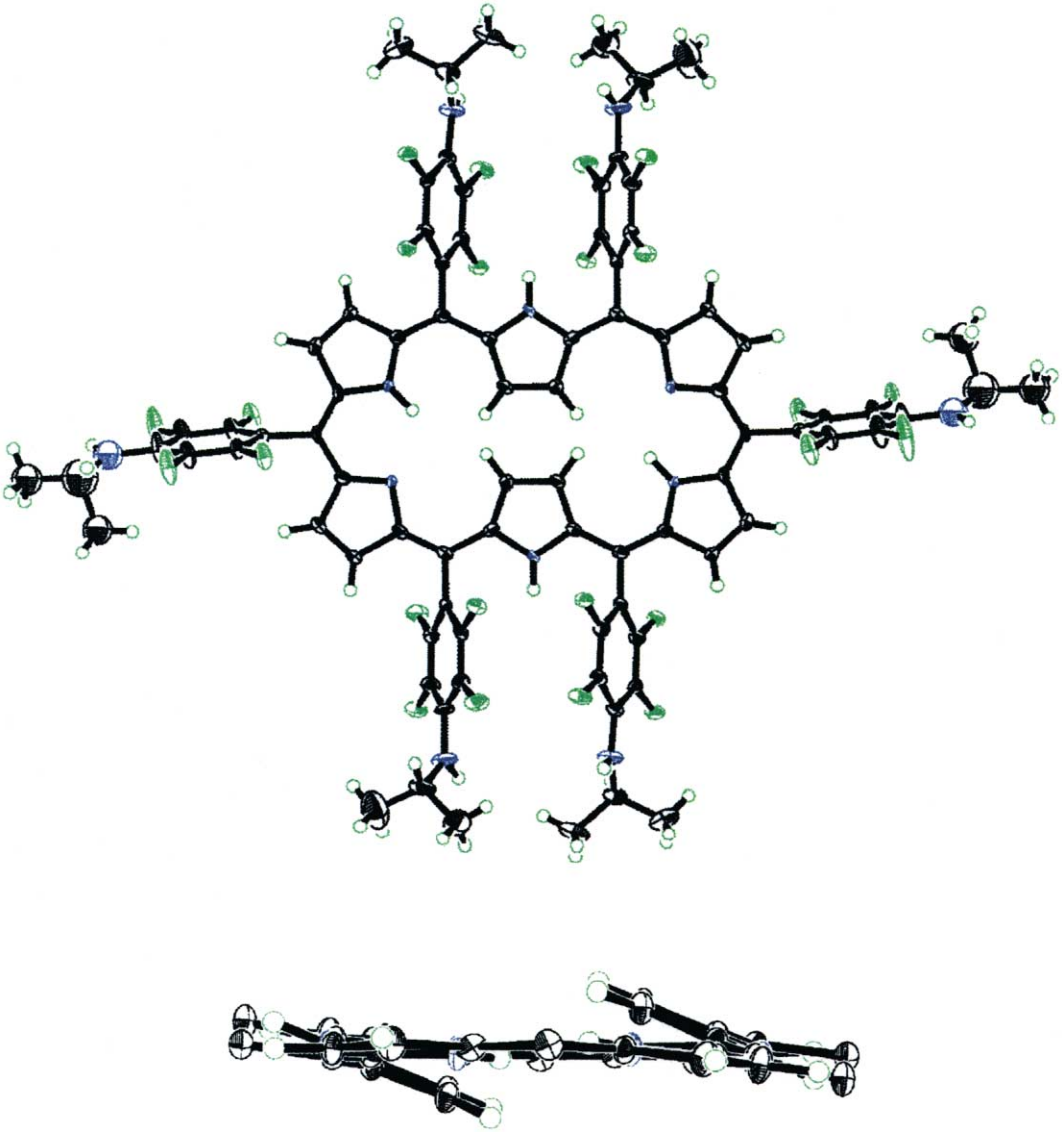

Figure 2. X-Ray crystal structure of **3**. Upper, top view; bottom, side view. In the side view, the *meso*-pentafluorophenyl substituents are omitted for clarity.

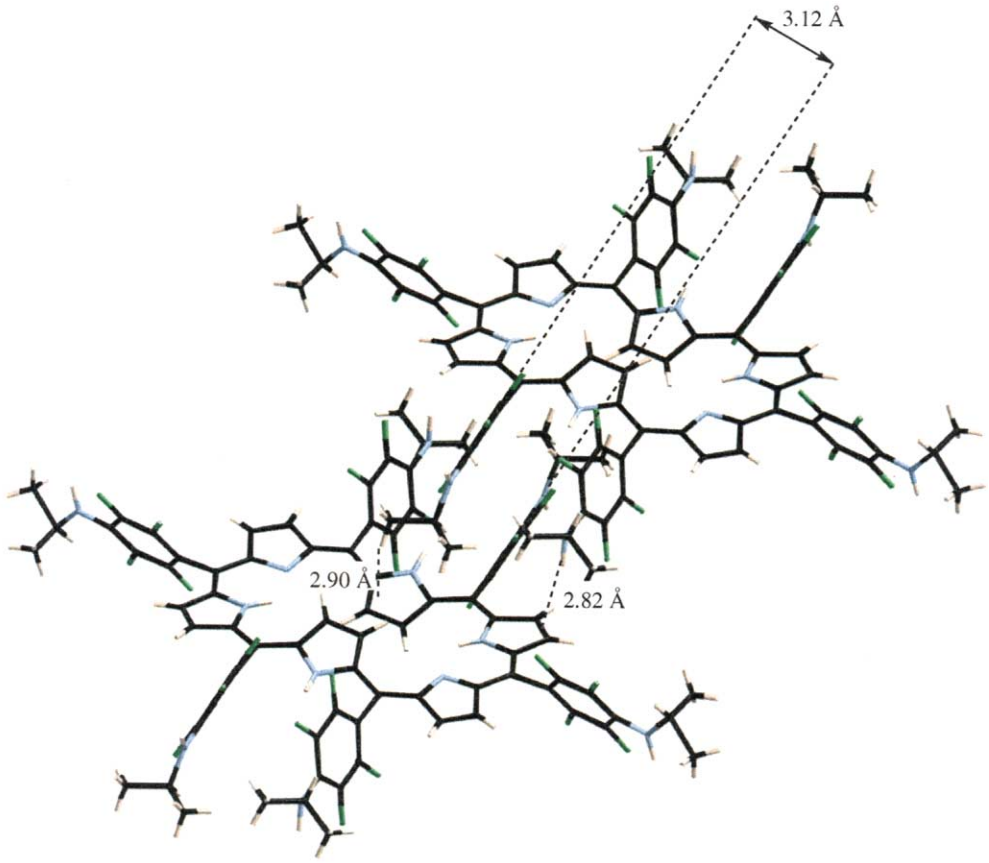

Figure 3. Crystal packing structure of **3**.

(Fig. 2) but this oxidized form is too insoluble to be characterized further. At the present stage, the origin of these partial aromatic character of [28]hexaphyrins is not clear but poses an interesting question with regard to the aromaticity of *meso*-aryl substituted hexaporphyrins. Figure 3 shows a crystal packing structure of **3**, where the neighboring [28]hexaphyrins are interacting through offset π–π interaction between the *meso*-substituted 4-isopropylamino-2,3,5,6-tetrafluorophenyl groups with an interplanar distance of 3.12 Å and the CH-π interaction between the methyl hydrogens in the isopropylamino group and the pyrrole ring with a distance of ca. 3 Å.

In summary, we explored the regioselective aromatic substitution reaction of the [26]hexaphyrin **1** with alcohols and isopropylamine, which provides a variety of hexaphyrins that are suited for their respective purposes. The X-ray crystal structure of **3** reported as the first example of [28]hexaphyrin indicates the similar rectangular shape as that of the oxidized form of [26]hexaphyrins and also sheds light on somewhat puzzling aromatic character of the reduced form of [28]hexaphyrin. Further studies on this interesting class of macrocycles are currently in progress in this laboratory.

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7. Analytical data for compound **3**; ^{1}H NMR (600 MHz, $CDCl_3$) $\delta = 1.25$ (s, 24H), 1.41 (s, 12H), 1.97 (s, 4H, inner β C–H), 3.38 (s, 2H, inner N–H), 3.72 (s, 4H), 3.86 (s, 2H), 4.00 (s, 4H), 4.19 (s, 2H), 7.71 (broad, 2H, outer N–H), 7.83 (s, 4H, outer β C–H), 7.93 (s, 4H, outer β C–H); FAB Mass $m/z = 1697$ (M^+), calcd for $C_{84}N_{12}H_{64}F_{24} = 1697$. Crystal data for **3**; $C_{84}N_{12}H_{64}F_{24}$ $M_r = 1696.5(0)$, triclinic, space group P-1, $a = 12.9059(1)$, $b = 13.9345(4)$, $c = 15.4276(2)$ Å, $\alpha = 92.925(1)$, $\beta = 112.885(1)$, $\gamma = 113.461(1)°$, $V = 2274.14(7)$ Å^3, $Z = 2$, $D_{calcd} = 1.377$ g/cm^3, $T = -150$°C, $R = 0.095$, $R_w = 0.133$, $GOF = 1.867$.