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Regioselective vicinal-dichlorination of *meso*-aryl [26]hexaphyrin(1.1.1.1.1.1)

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Abstract—Two synthetic methods are developed for halogenations of *meso*-hexakis(pentafluorophenyl)-substituted [26]hexaphyrin(1.1.1.1.1.1); one is regioselective trans-vicinal-dichlorination with sulfuryl chloride and the other is acid-assisted hydrohalogenation followed by oxidation with DDQ.

Electrophilic aromatic substitution reactions have been occupying the central position in organic chemistry, whereas it is known that polycyclic aromatic molecules such as naphthalenes,[1] anthracenes,[2] and phenanthrenes[3] undergo dihalogenation reactions under milder conditions, probably as a reflection of decreased aromatic stabilization energies compared with that of benzene. Porphyrins that are typical aromatic molecules as characterized by 18π-conjugated electronic networks undergo electrophilic substitution reactions similar to those of benzene derivatives.[4] These substitution reactions have been extensively used for modifications and functionalizations of porphyrins.

In recent years, expanded porphyrins that are constitutional homologs of porphyrin bearing more than five pyrrolic units have attracted considerable attention owing to their attractive optical, electrochemical, and coordination properties.[5] Yet, the chemistry of expanded porphyrins has still remained in its infant stage, leaving their chemical reactivities almost unexplored.[6] In this letter, we report peripheral halogenation reactions of *meso*-hexakis(pentafluorophenyl) substituted [26]hexaphyrin(1.1.1.1.1.1) **1**.[7] Purple [26]hexaphyrin **1** can be quantitatively converted to blue [28]hexaphyrin **2** by $NaBH_4$ reduction, while the oxidation of **2** with DDQ regenerates **1** quantitatively,[7] in contrast to porphyrins that exist solely as an aromatic 18π-electronic macrocycle.

In the course of our own studies on the photophysical properties of expanded porphyrin including **1**,[8] we found that irradiation (λ >300 nm, 500 W) of an aerated solution of **1** in CH_2Cl_2 for 10 min led to a clear change in the solution color from vivid purple to blue. From this reaction mixture, a product was isolated as green solids in 5–10% yield by silica gel column chromatography. This product was formed only by irradiation of **1** in chlorinated solvents such as CH_2Cl_2 and $CHCl_3$, but not in non-chlorinated solvents including toluene, acetone, and acetonitrile. This product exhibits the parent ion peak at $m/z = 1531.0171$ (calcd for $C_{66}H_{15}N_6F_{30}Cl_2$ $[M+H]^+$, 1531.0251) in high-resolution ESI-TOF-mass spectrum, indicating an addition of two chlorine atoms to **1**. The structure of this product has been unambiguously determined by single crystal X-ray diffraction analysis as trans-vicinal-dichlorinated hexaphyrin **3** (Fig. 1).[9] The product **3** shows an almost planar and rectangular macrocyclic shape with significant ruffling, in which the two chlorine atoms are attached to the inner β-positions in a trans manner (Fig. 1). The bond lengths of C(1)–C(2), C(2)–C(3), and C(3)–C(4) are in a range of 1.52–1.55 Å, hence indicating a single bond character. The bond lengths of C(2)–Cl(1) and C(3)–Cl(2) are 1.853(10) and 1.823(12) Å, respectively. The inverted pyrrole ring opposite to the dichlorinated pyrrole is very distorted with a large tilting angle of ca. 47.7° with respect to the mean plane of the hexaphyrin core, probably due to the steric repulsion of the

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Keywords: Expanded porphyrin; Hexaphyrin; Halogenation.

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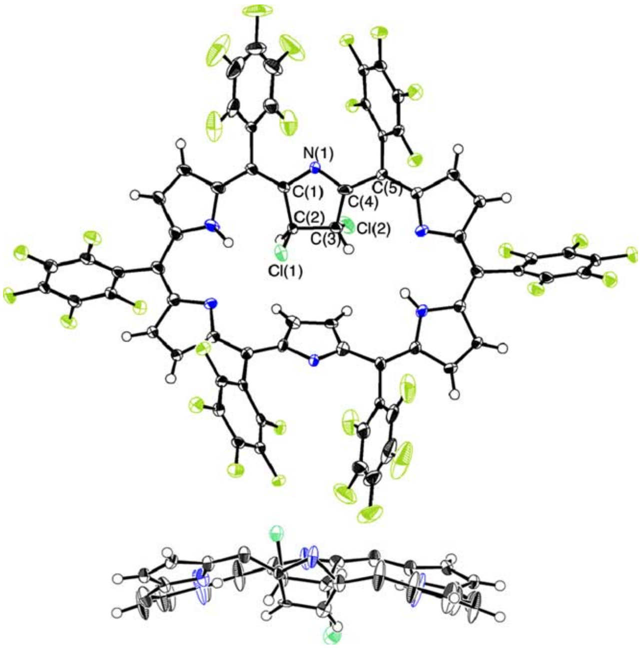


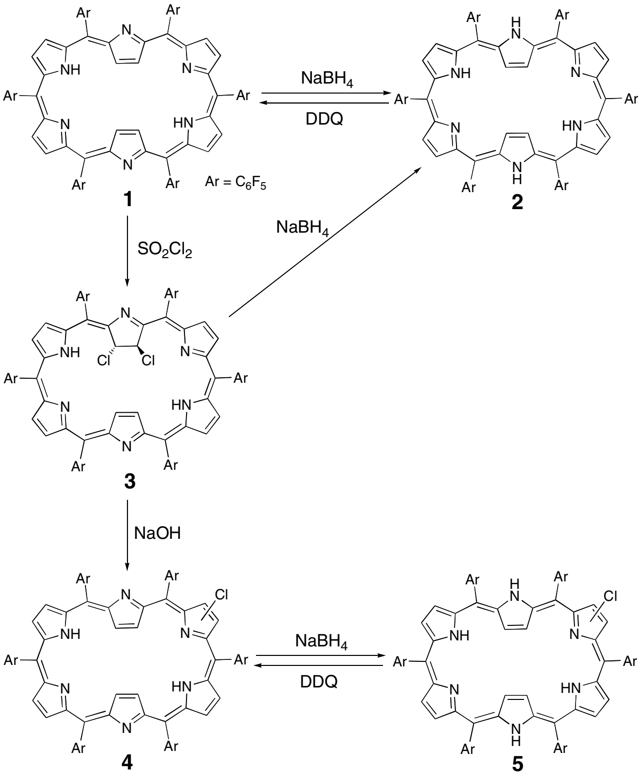
Figure 1. X-ray crystal structure of **3**: top view (top) and side view (bottom). Thermal ellipsoids are scaled to the 50% probability level. In the side view, *meso*-pentafluorophenyl groups are omitted for clarity.

substituted chlorine atoms. The ^{1}H NMR spectrum of **3** exhibits four doublets due to the outer β-protons in the range of 8.90–9.47 ppm, signals due to the inner β-protons of nonchlorinated and chlorinated pyrroles at −0.46 and −5.22 ppm, respectively, and a singlet at −1.78 ppm due to the inner NH protons, hence indicating the preservation of a strong diatropic ring current for **3**. The chloro-substituted sp^3 carbons were detected at 51.1 ppm in the ^{13}C NMR spectrum.

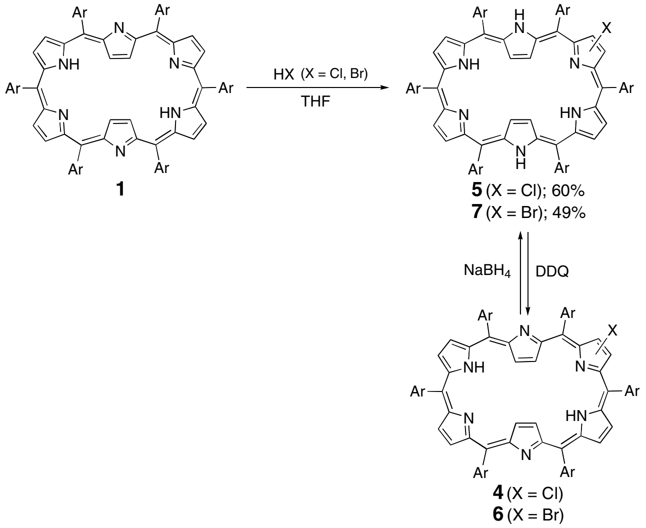
Since the peripheral halogenations of porphyrins were usually performed with halogenating agents such as *N*-bromosuccinimide (NBS), or *N*-chlorosuccinimide (NCS),[10] we attempted halogenations of **1** with these reagents, which failed to give any halogenated products. In the meanwhile, we found that the same dichlorination product **3** was prepared in 32% yield by the reaction of **1** with an equivalent amount of sulfuryl chloride in CH_2Cl_2 for 12 h at room temperature. In this reaction, monochloro[28]hexaphyrin **5** (31%) was isolated as a side product along with the unreacted [26]hexaphyrin **1** (∼20%). When more amounts of sulfuryl chloride were used, the reaction products became complicated including many polychlorinated products that were very difficult to separate. The observed regio-selectivity at the inner pyrrolic β-position is analogous to that of the Diels–Alder reaction of **1** with *o*-xylylene.[6c] High reactivity of the inner pyrrolic positions may be accounted for in terms of the large electron density of the HOMO orbital.[6c] Reductive dechlorination of **3** was quantitatively effected by treatment with $NaBH_4$ to give [28]-hexaphyrin **2**. When treated with sodium hydroxide, **3** underwent an elimination reaction to give monochlorinated [26]hexaphyrins **4** (∼40%), which exists as a mixture of three isomers (**4A**, **4B**, and **4C**) differing at the position of chloride, that is one at the inner pyrrolic position and two at the outer pyrrolic positions (vide infra, Scheme 1). On the other hand, the reaction of 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin with sulfuryl chloride under the same conditions led to a complicated mixture containing mono- and oligochlorinated porphyrins but vicinally dichlorinated chlorin products were not observed by ESI-TOF-mass spectrum.

The reversible redox interconversion between **1** and **2** is reminiscent of similar reactivity of quinones, which are known to undergo hydrochlorination with hydrochloric acid to give a chlorinated hydroquinone that can be oxidized to a chlorinated quinone. We, thus, examined hydrochlorination reaction of **1**. When stirred with excess amounts of concentrated hydrochloric acid in THF for 1 day at room temperature, the hexaphyrin **1** gave monochlorinated [28]hexaphyrin **5** (60%) and unsubstituted [28]hexaphyrin **2** (36%) along with small amounts of dichlorinated and oligochlorinated hexaphyrins (Scheme 2). Oligochlorinated side products may be produced via oxidation of monochlorinated [28]hexaphyrin **5**, whereas the formation of monochlorinated [28]hexaphyrin in the reaction with sulfuryl chloride may be ascribed to possible production of HCl from decomposition of sulfuryl chloride.

In contrast, **2** did not provide any hydrochlorination products under the same conditions. The ^{1}H NMR spectrum of **5** indicates that there exist three isomers differing in the position of chlorine atom, which were very difficult to separate, suggesting rapid caterpillar-motion

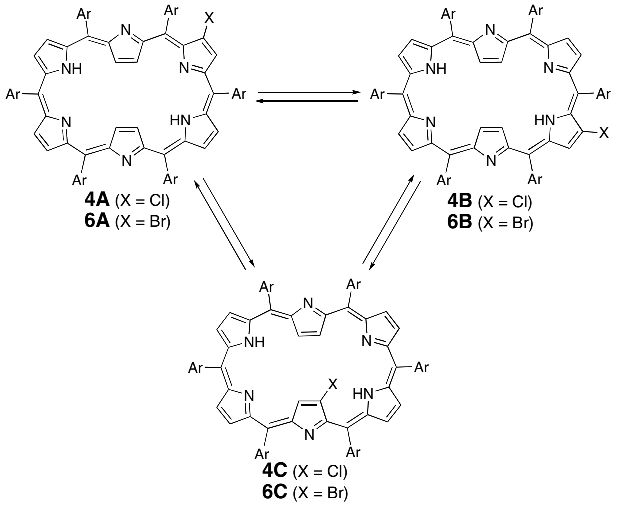


Scheme 1.



Scheme 2.

like rotational isomerization in **5**.[6d] On the other hand, the oxidized forms **4**, which were obtained by treating of **5** with DDQ or MnO_2, were found to exist as conformationally more stable isomers of **4A** and **4B** at room temperature, hence permitting their separation. Both the ^1H NMR spectra of **4A** and **4B** show sharp four doublet peaks due to the inner β-protons in the shielding region of −2.47 to −0.76 ppm and six doublets and one singlet peaks assigned to the outer β-protons appeared in the deshielded region of 8.68–9.47 ppm, suggesting their rectangular conformations. However, when the solutions of pure **4A** and **4B** were kept at room temperature for 1 day, ^1H NMR spectra of both compounds at room temperature became identical, displaying the thermodynamically equilibrated mixture consisting of **4A**, **4B**, and other isomer **4C** in the ratio of 1:1:0.2. This result can be well illustrated by the caterpillar-motion like rotational isomerization (Scheme 3), which has been revealed to be more facile for [28]hexaphyrins than [26]hexaphyrins.[6d]



Scheme 3.

A similar hydrobromination reaction was performed by treating **1** with hydrobromic acid in THF, which afforded monobrominated [28]hexaphyrin **7** in 49% yield. This product was quantitatively oxidized to monobrominated [26]hexaphyrins **6**, whose ^1H NMR spectrum showed the presence of three isomers, **6A**, **6B**, and **6C** that were actually separated. Both the ^1H NMR spectra of **6A** and **6B** show sharp four doublet peaks due to the inner β-protons in the shielding region of −2.45 to −0.52 ppm and six doublets and one singlet peaks assigned to the outer β-protons appeared in the deshielded region of 8.79–9.45 ppm. These products display ^1H NMR spectra and conformational stabilities similar to those of **4**, and the thermodynamic mixture has been revealed to consist of **6A**, **6B**, and **6C** in the ratio of 1.4:1.0:0.35.

In contrast to the relatively facile rotational isomerizations for the halogenated hexaphyrins **4** and **6**, the vicinally dichlorinated [26]hexaphyrin **3** is conformationally rigid up to 50 °C. On the ground of the conformational rigidity of **3**, we compared the optical properties of **3** with those of **1**. In $CHCl_3$, the absorption spectrum of **3** shows a Soret-like band at 569 nm and Q-like bands at 720, 779, 873, and 990 nm, which are slightly blue-shifted compared with those of **1** (Soret-like band at 567 nm and Q-like bands at 711, 768, 895, and 1025 nm). Recently, we reported the well-structured fluorescence emission from **1** as a rare case of

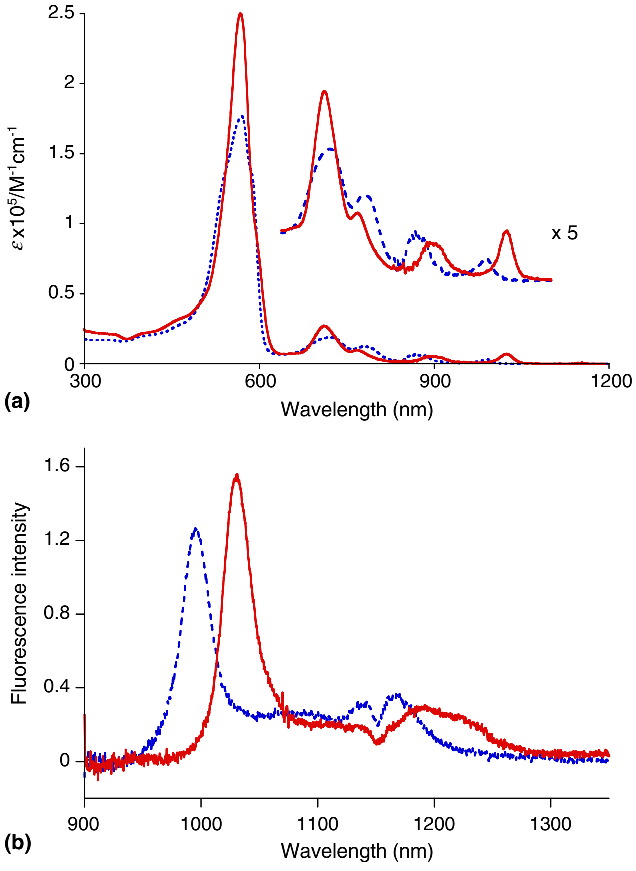


Figure 2. (a) Absorption and (b) fluorescence spectra (excited at 567 nm) of **1** (red, solid line) and **3** (blue, dotted line) in $CHCl_3$.

low-energy fluorescence.[8] The fluorescence spectrum of **3** shows a main peak at 995 nm, which is 36 nm blue-shifted compared with that of **1** (Fig. 2b). Stokes shift of **3** is only ca. 51 cm^{-1}, probably reflecting small structural changes from its excited state to the ground state that are similar to those of **1** that exhibits a Stokes shift of 57 cm^{-1}. The fluorescence intensity of **3** is reduced by only 20% as compared with that of **1**, despite the dichloro substituents.

In summary, two synthetic methods have been developed for the peripheral halogenations of [26]hexaphyrin **1**. One is the regioselective dichlorination with sulfuryl chloride to give trans-vicinal-dichlorinated hexaphyrin **3**, while the other is a sequence of hydrohalogenation and oxidation with DDQ to provide **4** and **6**. The latter method is useful for the preparation of mono-halogenated hexaphyrins. These methods will be useful for further fabrications of [26]hexaphyrins, allowing many possible preparations of functional molecules that incorporate a [26]hexaphyrin subunit.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.12.116.

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9. Crystal data for **3**: $C_{66}H_{14}N_6F_{30}Cl_2$, CH_2Cl_2; formula wt 1616.66, $T = 90(2)$ K, monoclinic, $C2/c$ (No. 15), $a = 38.845(13)$, $b = 5.9169(19)$, $c = 30.595(10)$ Å, $\beta = 121.915(5)°$, $V = 5969(3)$ Å^3, $Z = 4$, $D_{calcd} = 1.799$ g cm^{-3}, $\mu(\text{Mo K}\alpha) = 0.345$ mm^{-1}, $F(000) = 3192$, 17135 reflections measured, 6674 unique, $R1 = 0.0816$, $wR2 = 0.2314$, GOF = 1.026 ($I > 2.0\sigma(I)$). CCDC file no. 289048.
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