Expanded Porphyrins

A Doubly N-Fused Benzohexaphyrin and Its Rearrangement to a Fluorescent Macrocycle upon DDQ Oxidation**

Yasuhide Inokuma, Takahiro Matsunari, Noboru Ono, Hidemitsu Uno,* and Atsuhiro Osuka**

Over the past decade, much progress has been made in the expansion of π-conjugated porphyrinic electronic systems because of their potential applications as conductive materials, near-infrared (NIR) dyes, nonlinear optical materials, and photosensitizers for photodynamic therapy.[1–3] Representative examples include *meso*-ethynyl-substituted porphyrin oligomers[1] and multiply connecting porphyrin oligomers

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[*] Prof. Dr. N. Ono
Department of Chemistry, Faculty of Science
Ehime University
Bunkyo-cho 2-5, Matsuyama 790-8577 (Japan)
Fax: (+81) 89-927-9670
E-mail: ononbr@dpc.ehime-u.ac.jp
Prof. Dr. H. Uno
Integrated Center for Science
Ehime University
Bunkyo-cho 2-5, Matsuyama 790-8577 (Japan)
Fax: (+81) 89-927-9670
E-mail: uno@dpc.ehime-u.ac.jp
Y. Inokuma, T. Matsunari, Prof. Dr. A. Osuka
Department of Chemistry, Graduate School of Science
Kyoto University, and
Core Research for Evolutional Science and Technology (CREST)
Japan Science and Technology Agency
Sakyo-ku, Kyoto 606-8502 (Japan)
Fax: (+81) 75-753-3970
E-mail: osuka@kuchem.kyoto-u.ac.jp

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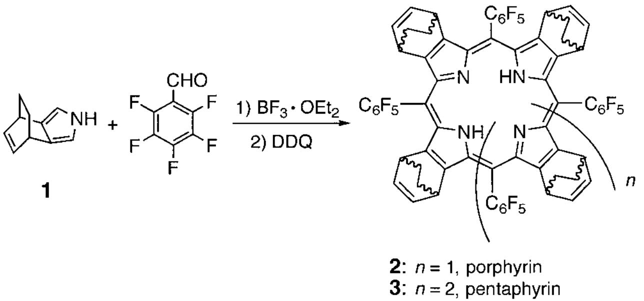
exemplified by *meso–meso*,β–β,β–β-triple-linked porphyrin arrays.[2,3] Another effective and promising synthetic strategy is the fusion of aromatic rings at the β-pyrrolic positions which can lead to a significant alternation in the electronic and optical properties through expansion of the π-electronic system as well as a change in the orbital symmetry.[4,5] This synthetic transformation has been made more feasible by using 4,7-dihydro-4,7-ethano-2*H*-isoindole (**1**, Scheme 1)[5a] as most of the synthetic steps can be performed without serious problems of solubility and a final retro-Diels–Alder reaction provides a benzoporphyrin quantitatively. Accordingly, various aromatic-fused porphyrins have been explored by this strategy.[5] Elsewhere, expanded porphyrins have recently emerged as a new class of oligopyrrolic macrocycle that exhibit unique optical and electrochemical properties as a result of their enlarged π-conjugated networks, which are larger than those of porphyrins.[6] Among these, we reported a series of *meso*-aryl expanded porphyrins prepared from the condensation reaction of pentafluorobenzaldehyde and pyrrole under modified Rothemund–Lindsey conditions.[7] Herein we report our attempts to apply the retro-Diels–Alder strategy to the synthesis of β-benzohexaphyrin-(1.1.1.1.1.1) using **1** as a key building block.

Following our protocol of *meso*-aryl-substituted expanded porphyrins,[7] a solution of **1** and pentafluorobenzaldehyde in CH_2Cl_2 (67 mM each) was treated with a catalytic amount of $BF_3{\cdot}OEt_2$ for 2 h, and the resulting mixture was oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) overnight (Scheme 1). Analysis by MALDI-TOF mass spectrometry of the reaction mixture revealed the formation of expanded porphyrins **3**–**6** as well as porphyrin **2**, each as products of retro-Diels–Alder reactions.

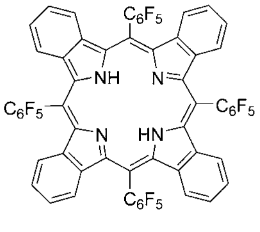


2: *n* = 1, porphyrin
3: *n* = 2, pentaphyrin
4: *n* = 3, hexaphyrin
5: *n* = 4, heptaphyrin
6: *n* = 5, octaphyrin

Scheme 1. Synthesis of porphyrins and expanded porphyrins.

Purification by column (silica gel) and gel-permeation chromatography led to the isolation of porphyrin **2**, pentaphyrin **3**, and hexaphyrin **4** in 18, 11, and 9.4% yield, respectively, as atropisomeric mixtures with respect to the orientation of the bicyclic rings.[8]

We then attempted retro-Diels–Alder reactions of **2** and **4**. Under the standard conditions (200 °C, 0.1 mmHg, 10 min), porphyrin **2** was quantitatively converted into tetrabenzoporphyrin **7**, which is green in color ($\lambda_{max} = 458$ nm in CH_2Cl_2) and displays a parent-ion peak at $m/z = 1175.1288$ in its high resolution electrospray-ionization time-of-flight (HR ESI-TOF) mass spectrum (calcd for $C_{60}H_{18}N_4F_{20}$: 1175.1285 $[M{+}H]^+$). Good-quality crystals of **7** in its diprotonated form were obtained which were suitable for analysis by X-ray diffraction.[9] The crystal structure shows a highly distorted saddle conformation with a dihedral angle between two opposite isoindole planes of 108.6° (Figure 1).



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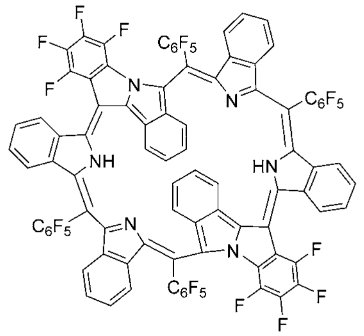

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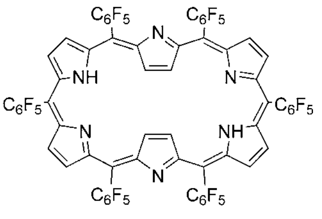

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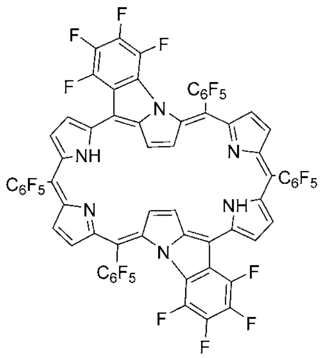

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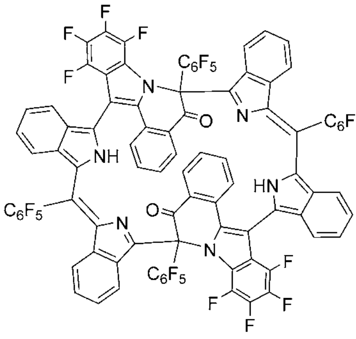

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Under the same retro-Diels–Alder reaction conditions, the hexaphyrin **4** gave an intractable complicated mixture, which contained multiply fluorine-eliminated products, as judged from MALDI-TOF mass spectra. But under milder retro-Diels–Alder conditions (170 °C, 0.1 mmHg, 30 min), **4** afforded a red–violet solid as the major product in 47% which has been assigned to the doubly N-fused β-benzo-[28]hexaphyrin(1.1.1.1.1.1) **8**. The HR ESI-TOF mass spectrum of **8** revealed a parent peak at $m/z = 1722.1767$ (calcd for $C_{90}H_{26}N_6F_{28}$: 1722.1766 $[M]^+$), and its ^1H NMR spectrum exhibited six doublets and six triplets in the range $\delta = 8.68$–6.16 ppm which are attibuted to the peripheral protons at the fused benzo moieties, and a broad signal at $\delta = 17.87$ ppm for

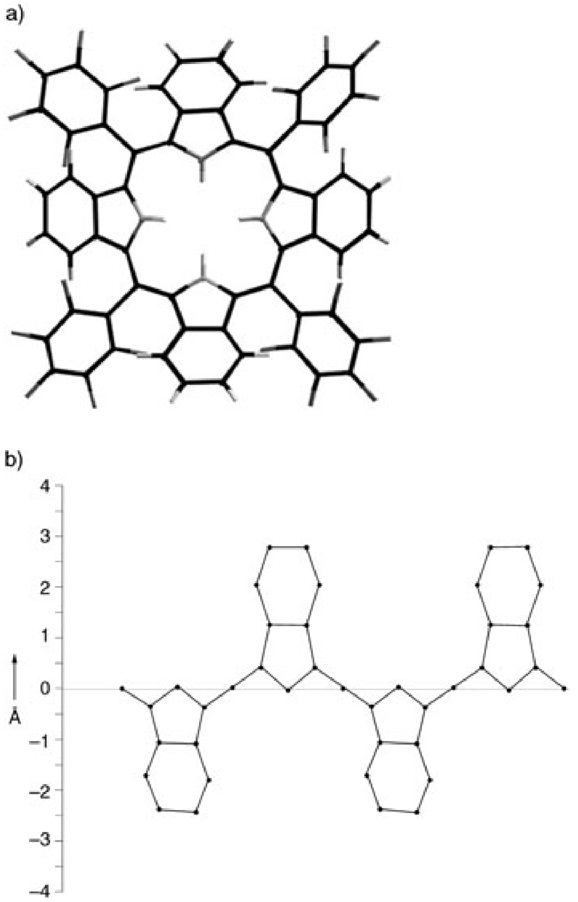

Figure 1. a) Crystal structure and b) skeletal deviation of tetrabenzoporphyrin **7**. Solvent molecules and counteranions (trifluoroacetate) are omitted for clarity.

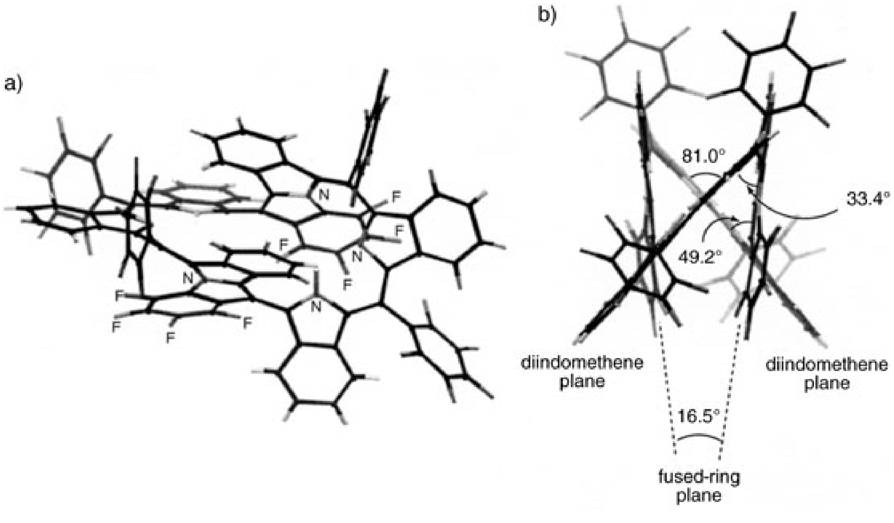

Figure 2. Crystal structure of **8**: a) top view, b) side view.

the inner NH protons. The downfield-shifted NH signal suggests hydrogen-bonding interactions. Overall these ^{1}H NMR data suggest nonaromatic character for **8**. The structure of **8** was confirmed by single-crystal X-ray diffraction analysis to be an *anti* doubly N-fused product from the expected benzohexaphyrin(1.1.1.1.1.1) (Figure 2),[10] which reveals a very strained structure that consists of two planar diindomethene and 11*H*-isoindolo[2,1-*a*]indole moieties with C_2 symmetry. The 11*H*-isoindolo[2,1-*a*]indole moieties are arranged in a near-parallel and face-to-face manner with an interplanar distance of 3.78 Å and a small dihedral angle of 16.5°, and are connected with diindomethene units with dihedral angles of 33.4° and 49.2°. The two planar diindomethene moieties are arranged in an almost perpendicular manner with a dihedral angle of 81.0°, despite the fully conjugated electronic system. As *anti* double-N-fusion of hexaphyrin can be effected upon heating a solution of hexaphyrin **9** in the presence of [Fe(acac)$_3$] (acac = acetylacetonate),[11] the thermal reaction of **9** (170 °C, 0.1 mmHg, 30 min) was carried out and merely gave a complicated mixture that contained a trace amount of **10**. This result suggests that the smooth *anti* double-N-fusion reaction observed for **4** is not general for hexaphyrins, but characteristic for β-benzohexaphyrin.

Next, the oxidation of **8** with DDQ was attempted to explore its two-electron-oxidized form. Addition of DDQ to a solution of **8** in CH$_2$Cl$_2$ led to clear spectral changes with isosbestic points (see Supporting Information) which suggest the formation of a complex between **8** and DDQ, but **8** was recovered quantitatively after the above solution was passed through a short column of alumina. A relatively low oxidation potential for **8** ($E_1 = 0.17$ V and $E_2 = 0.35$ V versus the ferrocene/ferrocenium (Fc/Fc$^+$) ion couple, as determined by cyclic voltammetry in acetonitrile) suggests a charge-transfer interaction for **8** and DDQ. This reaction was also monitored by ^{1}H NMR spectroscopy by using concentrated solutions of **8** (≥ 1 mM) and DDQ. Upon addition of 5 equivalents of DDQ to **8**, the ^{1}H NMR spectrum of **8** broadened and remained without substantial change for several hours. However, after 3 days, a clear and sharp spectrum was obtained from this sample which featured a single set of signals that indicate formation of a single major product. This change was accompanied by a distinct change in the color of the solution from red–purple to navy blue.

This oxidation reaction was then carried out on a preparative scale in the presence of a small amount of water to afford **11** in 48 % yield. The X-ray crystal structure of **11** was measured (Figure 3) and shows a C_2-symmetric structure that consists of two planar diindomethene and isoindolo[2,1-*a*]isoquinolin-5-one subunits.[12] Interestingly, the resulting two sp^3-hybridized carbon atoms that connect these two subunits serve to interrupt the conjugation of the macrocycle. In the structure of **11**, the two diindomethene moieties are

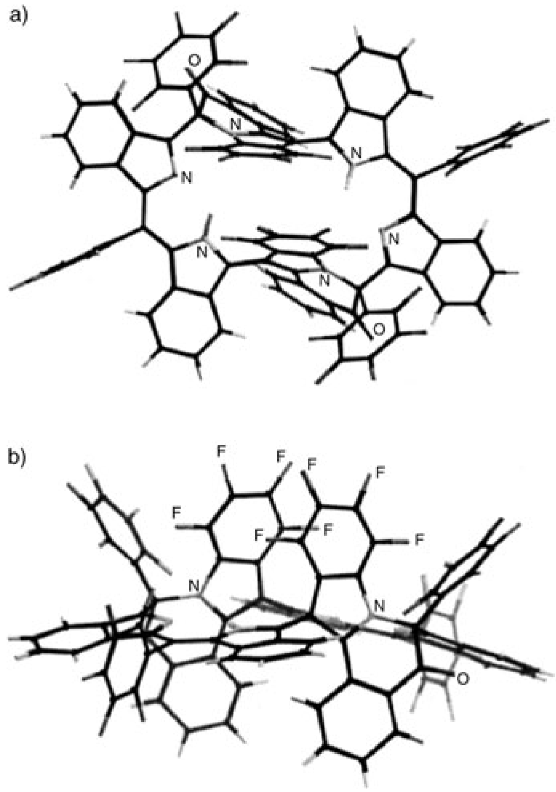

Figure 3. Crystal structure of **11**: a) top view, b) side view.

arranged in a roughly coplanar arrangement (dihedral angle 30.8°) to which the isoindolo[2,1-*a*]isoquinolin-5-one moieties are placed with dihedral angles of 69.2° and 81.4°. The spectral data for **11** are fully consistent with this unique structure: HR ESI-TOF mass spectroscopy revealed a parent-ion peak at $m/z = 1755.1732$ (calcd for $H_{90}H_{27}N_6F_{28}O_2$: 1755.1743 $[M+H]^+$), and ^{13}C NMR spectroscopy showed signals at $\delta = 186.2$ and 37.3 ppm which correspond to carbonyl and sp^3-hybridized carbon atoms, respectively. When this oxidation was performed in the presence of $H_2{}^{18}O$, the oxygen atoms of the carbonyl group were enriched with ^{18}O, which suggests adventitious water as a source of oxygen atoms. A similar oxidation reaction was attempted for *anti* double-N-fused hexaphyrin **10** under the same conditions. Although similar spectral changes were observed upon addition of DDQ in CH_2Cl_2, **10** was recovered quantitatively from the reaction mixture at high concentration, which suggests that this oxidative rearrangement is unique to a doubly N-fused benzohexaphyrin substrate, plausibly being triggered by its severe strain.

The absorption spectra of **8** and **11** differ significantly from each other (Figure 4), which reflect skeletal rearrangements and disruption of the electronic conjugation. Whereas **8** is virtually nonfluorescent in most of the solvents examined, **11** emits relatively strong fluorescence in nonpolar solvents. As shown in Figure 4, the fluorescence emission of **11** is observed at $\lambda = 718$ nm ($\lambda_{ex} = 578$ nm), with a large Stokes shift and a quantum yield of $\Phi_F = 0.034$ in CH_2Cl_2 with respect to that of methylene blue ($\Phi_F = 0.035$ in methanol).[13] The fluorescence of **11** can be thought to originate from a diindomethene subunit, according to a recent report on a series of related boron–diindomethene dyes,[14] but its substantial shift to longer wavelengths is noteworthy and can be accounted for in terms of conjugation with an isoquinolin-5-one subunit. The relatively high quantum yield of fluorescence for **11** is attractive as fluorescence in this near-IR region (650–900 nm) is quite useful for a variety of applications including biochemical fluorescence imaging and sensing,[15] despite a limited number of fluorescent dyes in this region known.[16] Furthermore, the fluorescence of **11** is quite dependent on solvent polarity and its fluorescent quantum yield decreases with increasing solvent polarity: $\Phi_F = 0.056$ in chlorobenzene, 0.054 in toluene, 0.048 in benzene, 0.033 in ethyl acetate, 0.029 in tetrahydrofuran, 0.013 in pyridine, 0.008 in benzonitrile, 0.004 in acetone, 0.002 in methanol, and less than 10^{-3} in nitromethane, *N*,*N*-dimethylformamide, and acetonitrile, in parallel to the reported trend of polar diindomethene dyes.[14] The quenching of the fluorescence of **11** is indeed dependent on the polarity of the bulk solvent, but not on specific molecular interaction with polar solvent molecules, as revealed by experiments in mixed solvent systems, CH_2Cl_2/acetonitrile and toluene/nitromethane. These results are encouraging for the potential use of **11** as a polarity indicator in complicated environments.

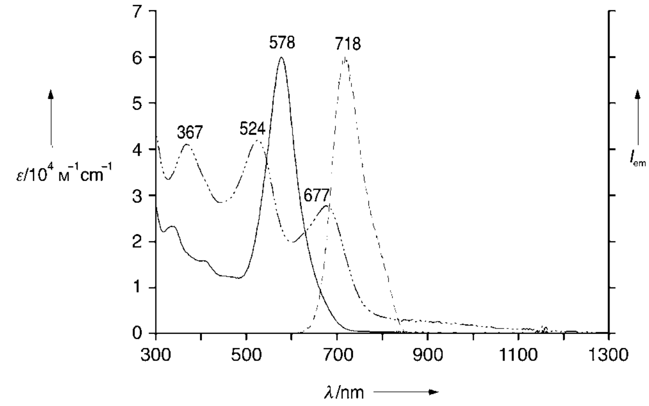

Figure 4. UV/Vis absorption spectra of **8** (–•–•) and **11** (——), and the fluorescence emission spectrum of **11** (– – –, $\lambda_{ex} = 578$ nm) in CH_2Cl_2.

In summary, doubly N-fused β-benzo[28]hexaphyrin-(1.1.1.1.1.1) **8** was synthesized as the first example of a β-benzo-expanded porphyrin through the retro-Diels–Alder reaction of a β-bicyclo[2.2.2]octadiene-fused hexaphyrin. The molecule **8** undergoes an oxidative rearrangement to macrocycle **11**, which emits fluorescence that is dependent on the polarity of the solvent. Extension of this synthetic strategy to larger expanded porphyrins is currently in progress in our laboratory.

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[8] MALDI-TOF mass spectrometry revealed the formation of heptaphyrin **5** ($m/z = 2055$, calcd for $C_{105}H_{32}F_{35}N_7$:2055.2) and octaphyrin **6** ($m/z = 2353$, calcd for $C_{120}H_{38}F_{40}N_8$:2350.3). A retro-Diels–Alder reaction occurred under laser-irradiation to produce a benzo skeleton from a bicyclo one. These products could not be isolated owing to low yields and overlapping R_f values in TLC.

[9] Crystal data for the diprotonated form of tetrabenzoporphyrin **7**: monoclinic, space group $C2/c$ (no. 15), $a = 20.91(3)$, $b = 20.76(3)$, $c = 15.87(2)$ Å, $\beta = 102.26(6)°$, $V = 6732(17)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.690$ g cm^{-3}, $T = 123$ K, crystal size $0.50 \times 0.40 \times 0.20$ mm^3, $R = 0.085$, $R_w = 0.241$, GOF = 1.363 with $I > 2.00\sigma(I)$. CCDC 257492 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[10] Crystal data for **8**: orthorhombic, space group $C222_1$ (no. 20), $a = 20.06(3)$, $b = 26.20(2)$, $c = 16.36(1)$ Å, $V = 8595(14)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.398$ g cm^{-3}, $T = 123$ K, crystal size $0.25 \times 0.10 \times 0.05$ mm^3, $R = 0.061$, $R_w = 0.085$, GOF = 0.861 with $I > 3.00\sigma(I)$. CCDC 257493 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[12] Crystal data for **11**: orthorhombic, space group $Pbcn$ (no. 60), $a = 22.78(2)$, $b = 21.31(1)$, $c = 20.26(1)$ Å, $V = 9837(11)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.547$ g cm^{-3}, $T = 123$ K, crystal size $0.60 \times 0.20 \times 0.10$ mm^3, $R = 0.069$, $R_w = 0.105$, GOF = 0.839 with $I > 3.00\sigma(I)$. CCDC 257494 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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