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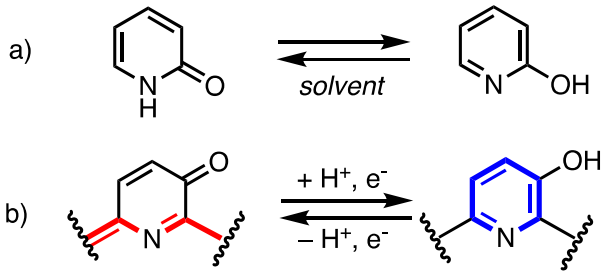
Reversible Redox System of 2-Oxypyritriphyrin(1.2.1) Accompanying Interconversion between 3-Pyridone and 3-Hydroxypyridine Units

Su-Gi Chong[a], Tomoki Yoneda[a]*, Yuki Ide[b], and Saburo Neya[c]*

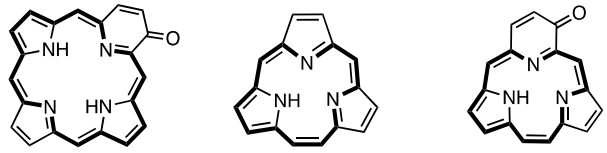
Abstract: To develop a system in which a π-conjugation circuit switched by a redox reaction between 3-pyridone and 3-hydroxypyridine, a ring-contracted analog of oxypyriporphyrin, 2-oxypyritriphyrin(1.2.1) was synthesized for the first time. 2-Oxypyritriphyrin(1.2.1) contains a 14π aromatic conjugation circuit with the keto-form of the 3-oxypyridine ring. When 2-oxypyritriphyrin was treated with $NaBH_4$, not only the 3-oxypyridine group, but also the *meso*-carbons were also reduced to give a colorless porphyrinogen analog. The reduced compound could be oxidized again to provide 2-oxypyriporpyhrin in a reversible manner.

Switching the π-conjugation of a structure is important for the control of their optical, electronic, and chemical properties.[1] In particular, there has been considerable research into controlling the aromatic conjugated structures of macrocycles because of their rich optical and electronic properties. One example of such drastic interconversions is switching of aromaticity of expanded porphyrins[2a] and N-confused porphyrins[2b], which sometimes accompanies the topological change or tautomerism of pyrrole units. However, even considering these molecules, a general methodology for the design of switchable macrocycle has not been efficiently developed.

To construct a simple system for switching a π-conjugation circuit, we investigated the interconversion between 3-pyridone and 3-hydroxypyridine incorporated into porphyrinoids. The interconversion of 3-pyridone and 3-hydroxypyridine is different from those of 2- and 4-pyridones and hydroxypyridines. The equilibrium between 2- and 4-pyridones and hydroxypyridines is controlled by the polarity of the solvents.[3] The interconversion between their NH- and OH- forms occurs without any generation of charged atoms (Scheme 1a). In contrast, 3-oxypyridine cannot take the keto-form because of its non-Kekulé structure.[4] However, when the 3-oxypyridine unit is connected to a π-conjugation circuit, the keto-form of the 3-oxypyridine unit can be reduced to 3-hydroxypyridine (Scheme 1b). Therefore, if the interconversion of a 3-pyridone unit is incorporated into a macrocycle, the macrocyclic conjugation could be controlled with high reliability.



Scheme 1. Interconversion between hydroxypyridines and pyridones; a) tautomerism of 2-hydroxypyridine and 2-pyridone and b)interconversion of 3-oxypyridine with π-conjugation induced by a redox system.



Oxypyriporphyrin **Triphyrin(2.1.1)** **2-Oxypyritriphyrin(1.2.1)**

Figure 1. Chemical structures of oxypyriporphyrin, triphyrin(2.1.1), and 2-oxypyritriphyrin**.** The aromatic conjugation circuits are shown in bold lines.

Oxypyriporphyrin[5] (Figure 1), which incorporates a 3-pyridone unit into a porphyrin, is a candidate for such a macrocycle. However, oxypyriporphyrin has not been reported to display any such interconversion because of the strong hydrogen bonding network of the 18π aromatic conjugation circuit. Protonation by trifluoroacetic acid of the 3-oxypyridine unit in the pyriporphyrin system has resulted in batho- and hyperchromic-shifts of Soret and Q bands being observed. But in these cases, the 18π aromatic conjugation circuit of the oxypyriporphyin was preserved.[5a]

To achieve the interconversion between aromatic conjugation circuits, a porphyrinoid with weaker intramolecular hydrogen bonds than those of oxypyriporphyrin is required. In a study of equilibrium of 3-oxypyridine embedded porphyrinoids, we recently reported the interconversion of aromaticity of 3-oxypyripentaphyrin(0.1.1.1.0).[6] 3-Oxypyridine indicated remarkable solvatochromism especially in protic solvents such as

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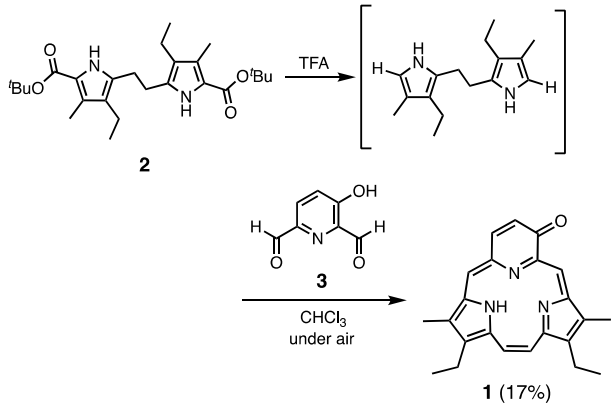
methanol. This system shows the possibility of definite interconversion between 3-pyridone and 3-hydroxypyridine, which affects the aromaticity of macrocycles accompanying the alternation of the number of inward-pointing NH protons.

Herein, we report the synthesis of ring-contracted 2-oxypyritriphyrin(1.2.1), which has a moderate internal hydrogen bonding network derived from its three nitrogen atoms. The all-pyrrole analogue of triphyrin(2.1.1)[7] was first synthesized by Xue, Shen, Yamada, You, and Kobayashi *et al.*, by the acid-catalyzed condensation of reaction of pyrrole[7a-c] and has also been synthesized by McMurry coupling of di-formylated tripyrrane.[7d] These triphyrins show aromaticity derived from its 14π aromatic conjugation circuit and have hydrogen bonding in the 1,2-bipyrroleethene unit. Its 14π aromatic conjugation circuit displays high planarity. In addition, in the case of thiatriphyrin[8], the number of NH protons in the ethylene-bridged pyrroles can be not only one, but zero or two.

The synthetic route of 2-oxypyritriphyrin **1** was the acid-catalyzed condensation of 1,2-bis-(5-butoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)-ethane **2**, which was prepared by the homocoupling[9] of 2-acetoxymethyl-3-ethyl-4-methyl-5-butoxycarbonylpyrrole, and 2,6-diformyl-3-hydroxypyridine **3**. The *tert*-butoxycarbonyl group of **2** was removed in trifluoroacetic acid before condensation with 2,6-diformyl-3-hydroxypyridine[10] in chloroform under reflux conditions. The condensed macrocycle was automatically oxidized under aerobic conditions to yield 2-oxypyritriphyrin(1.2.1) **1** as red solids in 17% yield (Scheme 2).



Scheme 2. Synthesis of 2-oxypyritriphyrin(2.1.1) **1.**

Analysis of the characterization data of **1** indicated its keto-form with 14π aromatic character. High-resolution electrospray ionization mass spectroscopy (HR-ESI-TOF-MS) provided the parent ion peak of **1** at *m/z* = 380.1737 (calcd for $C_{23}H_{23}ON_3Na^+$ [*M*+Na]$^+$: 380.1733). The ^{1}H NMR chemical shifts of **1** indicated aromatic character, including the downfield shifted peaks of the *meso* protons at 9.59 and 8.84 ppm. The peaks for the vinylene bridge, observed at 8.93 and 8.89 ppm, were also downfield shifted. The signals of protons at β and γ positions of the pyridone groups were observed at 8.54 and 7.40 ppm as doublet with coupling constant *J* = 9.6 Hz, reflecting an enone character rather than the aromatic pyridine ring. The peak of the inner NH proton was observed at 8.74 ppm, because of the valence of the hydrogen bonding and diamagnetic ring current. The^{13}C NMR spectrum of **1** displayed a signal of ^{13}C belonging to carbonyl group at 183.5 ppm. In the infrared spectrum, a peak at 1609 cm^{-1}, which is derived from the carbonyl C=O double bond was also observed.

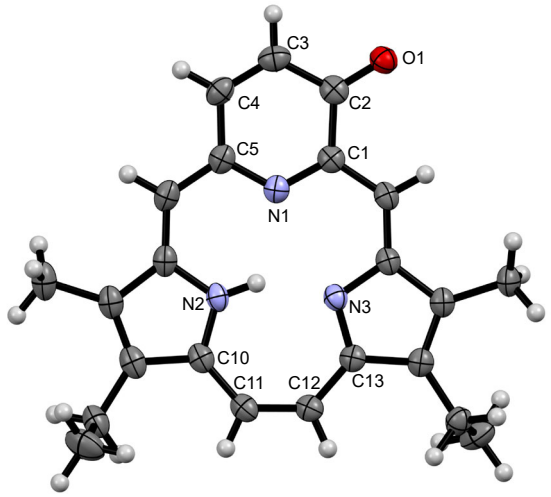
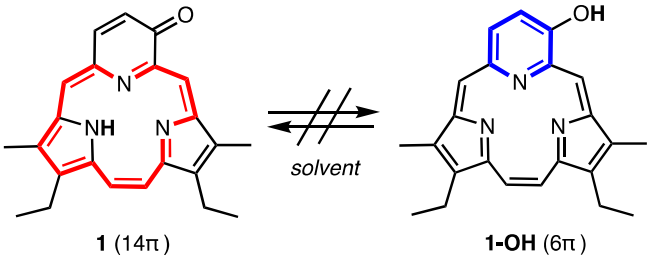


Figure 2. X-Ray crystal structure of **1.** Thermal ellipsoids set at 50% probability. The miner disorder component was omitted for clarity.

A single crystal of **1** was obtained by slow diffusion of heptane into a carbon tetrachloride solution of **1** and the structure was unambiguously determined by X-ray crystallographic analysis[11] (Figure 2). The overall structure was almost planar with a mean plane deviation (MPD) of 0.02 Å (average distance of core 20 atoms from their mean plane). The C2–O1 distance was 1.2364(19) Å, supporting the double bond character. The bond alternation was also clearly observed in the peripheral C–C bonds, 1.477(2), 1.444(2), and 1.447(2) Å for the C1–C2, C2–C3 and C4–C5 single bonds and 1.354(2) Å for the C3–C4 double bond. In contrast, almost no bond-length alternation was observed between 1.3336(19) and 1.3335(19) Å of N1–C1 and N1-C5 bond, respectively, which strongly suggested their aromatic bond character. The lengths of the C11-C12 [1.390(2) Å], C10–C11 [1.410(2) Å] and C12–C13 [1.411(2) Å] bonds around the vinylene bridge also suggest their aromatic bond character. The harmonic oscillator model of aromaticity (HOMA)[12] value for the overall 14π macrocyclic structure of **1** was 0.64, which also indicated the aromatic character of the macrocycle (See SI).

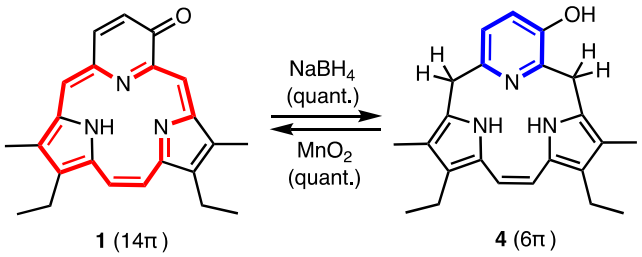


Scheme 3. Keto-enol tautomerization of 2-oxypyritriphyrin **1**.

The keto-conformation of the 3-pyridone unit of **1** was preserved regardless of the solvent in methanol, acetone, acetonitrile, DMSO, dichloromethane, toluene, and hexane, as assessed by the UV/Vis absorption spectra (See SI). This fact suggested that solvatochromic pyridone-hydroxypyridine interconversion of 3-oxypyridine does not occur (Scheme 3). **1-OH**, the tautomeric state of **1**, has three iminic nitrogens, which may cause severe steric repulsion of the unpaired electrons.

Next, we investigated the direct reduction of the 3-pyridone unit to provide the 3-hydroxypyridine unit (Scheme 4). When **1** was mixed with excess $NaBH_4$ in THF, the pink color of **1** was smoothly changed to green, but to our surprise, the color of **1** was

quickly faded into pale yellow. After work-up, we obtained the reduced product **4** quantitatively (Scheme 4, right arrow). The HR-ESI-TOF-MS spectrum of **4** displays the parent peak at *m/z* = 360.2084 (calcd for $C_{23}H_{23}ON_3^-$ [*M*–H]$^-$: 360.2081), indicating addition of four hydrogen atoms to **1** by reduction. The ^{1}H NMR spectrum of **4** showed two upfield-shifted 2H singlets at 4.07 and 3.93 ppm, indicating the presence of aliphatic methylene units. (Figure 3b) The signals of the *meso*-protons of **1** in the aromatic region was disappeared, suggesting that the sp^2 *meso*-carbons was reduced to sp^3 carbons. The signals for protons of the vinylene and pyridyl groups were also upfield-shifted compared with those in **1**. In ^{13}C NMR spectrum, two more signals derived from sp^3 carbons were observed compared with **1** and a downfield-shifted signal for a carbonyl group (> 160 ppm) were not observed. From these data, we concluded that four-proton and four-electron reduction of **1** was proceeded to provide **4** with two *meso*-sp^3 CH_2 carbons. (Scheme 4).



Scheme 4. Reversible interconversion between **1** and **4**. Aromatic conjugation circuits are shown in bold lines.

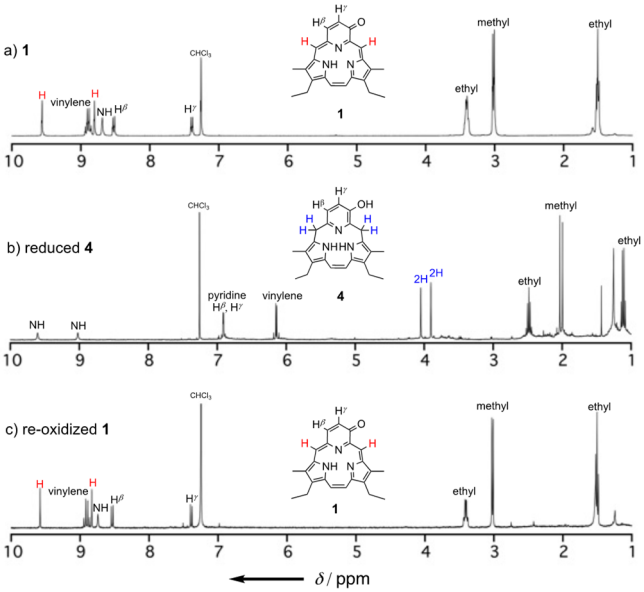


Figure 3. ^{1}H NMR spectra of a) **1**, and b) reduced crude product containing **4**, and c) re-oxidized reaction mixture.

In the UV/Vis absorption spectrum, the absorption peak of **4** was shown at 348 nm and the longest absorption wavelengths were below 500 nm, strongly supporting a shortened π-conjugation circuit (Figure 4). When the reaction was performed in a cuvette with a 17 μM THF solution of **1**, the pink color of **1** was almost completely changed to a colorless solution.

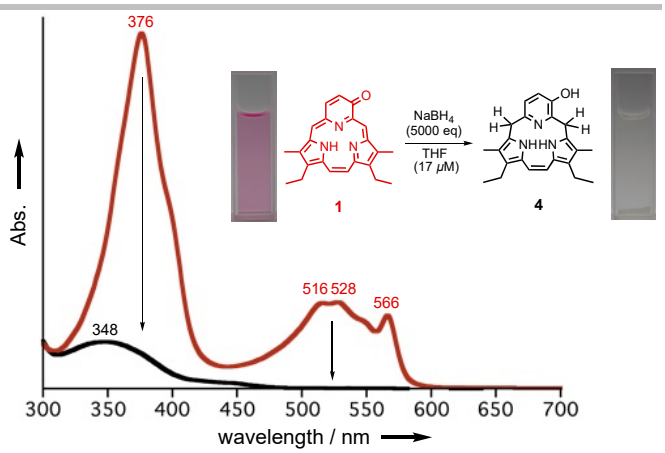
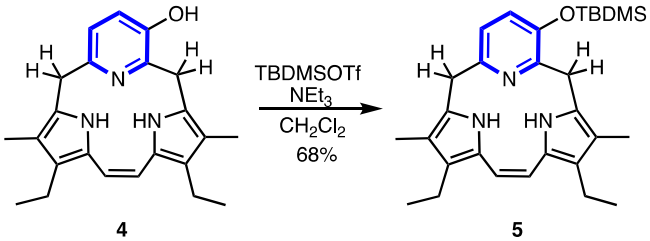


Figure 4. UV/Vis Absorption spectra of **1** and **4** in THF**.** The photographs show the optical color change of a THF solution of **1** and **4** (17 μM).

The reversibility of the reduction was confirmed by the re-oxidation of **4**. When the re-oxidation of **4** was performed with 10 equivalents of MnO_2, **1** was recovered quantitatively (Scheme 4, left arrow). The peaks of **4** were almost completely altered to those of **1** (Figure 3c). In addition, in $CDCl_3$, **4** was also gradually oxidized to **1** under aerobic conditions. The signals of **1** slowly appeared in a $CDCl_3$ solution of **4** over 48 h (See SI), and the pink color of solution became deeper.

We tried to protect the hydroxy group of **4** because the complete purification of **4** by silica-gel column chromatography was hampered by the smooth oxidation of **4** in air. We supposed that when the hydroxy group of **4** was protected, the oxidation pathway accompanying the oxidative ketonization to **1** would be blocked. After some trial and error experiments, we found that *tert*-butyldimethylsilyl (TBDMS) triflate was suitable for protection of the hydroxy group. We managed to separate the TBDMS-protected compound **5** in 68% yield by silica-gel column chromatography albeit some deprotection on silica-gel was observed. In the ^{1}H NMR spectrum of **5**, all protons were only slightly shifted from that of **4** except for peaks derived from the *tert*-butyldimethylsilyl group. The stability of isolated **5** was increased compared with that of **1**, although **5** was slowly oxidized in $CDCl_3$ solution and under aerobic conditions (about 10% of **5** in $CDCl_3$ was oxidized to **1** in 48 h).



Scheme 5. Protection of hydroxy group of **5** with *tert*-butyldimethylsilyl group.

While the mechanism for the reduction is not clear at this stage, this reduction is likely to be initiated by conjugative reduction of *meso*-position of **1** accompanying the reduction of the 3-pyridone unit to the 3-hydroxypyridine unit. The second reduction is then triggered by the re-aromatization of the pyrrole units. (See SI)

In summary, we have constructed a 3-oxypyridine embedded triphyrin(1.2.1) as a macrocycle with conjugation that could be switched by redox reaction with the mild reductant $NaBH_4$ and the

mild oxidant MnO_2. The aromatic system of the 14π conjugation circuit of **1** could be disconnected, accompanying reduction of the sp^2 carbons and 3-pyridone unit to 3-hydroxypyridine unit. A drastic optical property change was observed by disconnection of the π-conjugation circuit of **1**. The reduced product could be smoothly oxidized again to afford the macrocycle **1** with 3-pyridone unit in a reversible manner. Considering that many macrocyclic aromatic molecules are currently available, the development of a general methodology to enable conjugation-state switching is of high importance. Therefore, such reversible redox-promoted systems using the 3-pyridone unit have the potential for application of other π-conjugated molecules.

Acknowledgements

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Keywords: Pyridone • Redox System • Porphyrin • Triphyrin • Pyriporphyrin

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[11] X-Ray crystallographic data for **1**: $C_{23}H_{23}N_3O$ (M_r = 357.44), tetragonal, space group $P4_2/n$, a = b = 23.1090(6), c = 6.9478(3) Å, V = 3710.3(3) Å^3, Z = 8, ρ_{calcd} = 1.280 gcm^{-3}, T = 123(2) K, R_1 = 0.0415 ($I > 2\sigma(I)$), wR_2 = 0.1060 (all data), GOF = 0.1033. CCDC 2063273 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the Cambridge Crystallographic Data Centre.

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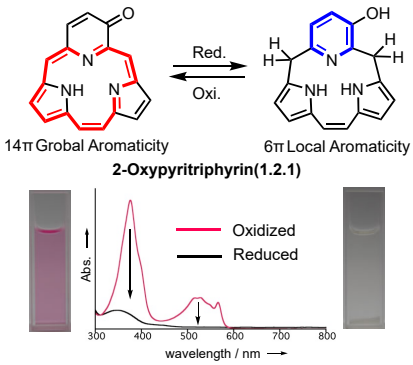

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