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Macrocycle Contraction and Expansion of a Dihydrosapphyrin Isomer

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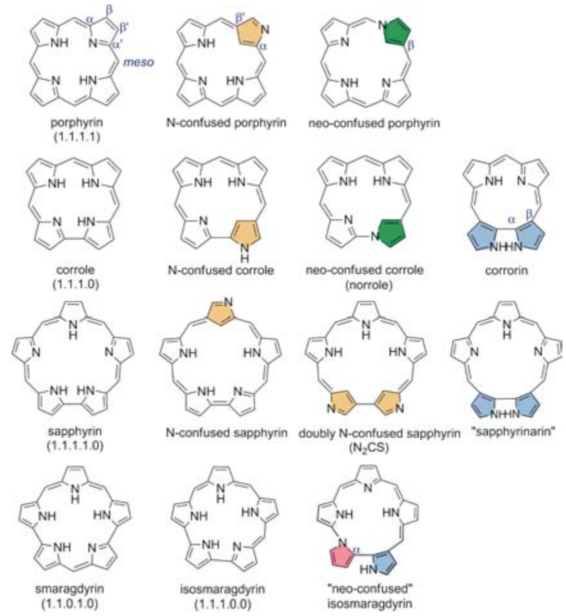
Supporting Information

ABSTRACT: Cyclization of a pentapyrrane with two terminal β-linked pyrroles afforded a dihydrosapphyrin isomer (**1**) with the pyrroles linked in a unique $\beta,\alpha-\alpha,\beta$ mode, which was rather reactive, and thus it readily underwent a ring-contracted rearrangement to a pyrrolyl norrole (**2**), and succeeding ring expansion to a terpyrrole-containing isosmaragdyrin analogue (**4**). **1**, **2**, and **4** contain the internal ring pathways with a minimum of 17, 15, and 16 atoms, respectively. **1**, **2**, and **4** are almost nonfluorescent, whereas the complex of **2** with Zn^{2+} shows a distinct NIR emission peak at 741 nm. The unprecedented pyrrole transformation chemistry by confusion approach is illustrated.

Macrocyclic frameworks widely occur in nature. The development of novel macrocycles with specific functionality has long been an interesting research topic for chemists.[1] In recent years, porphyrins and porphyrin analogues have attracted considerable attention due to their versatile structures and properties.[2] Among them, the pyrrole-mislinked isomers of porphyrin as well as their contracted and expanded families are of particular interest because they could provide diversity in structures and properties. Typical examples include N-confused porphyrin,[3] neo-confused porphyrin,[4] neo-confused corrole (norrole),[5] corrorin,[6] and hexaphyrins with multiple N-confused pyrroles,[7] in which one or more pyrrole rings are connected through the α,β' (confused), α,β, or N,β (neo-confused) positions (Chart 1).[4,5] The stability differs largely among the different isomers, and transformation into the other types of macrocycles, such as N-fused porphyrin, N-fused sapphyrin, doubly N-confused hexaphyrin, etc., has occasionally been observed.[6a,8] As both the isomers and transformed macrocycles exhibit unique properties and display different functions compared with their parent compounds, installing of confused (or mislinked) pyrroles into the macrocyclic frameworks, which we call *confusion approach*, is becoming one of the promising synthetic strategies to access to the novel porphyrinoids with worthy features.[9] Herein, we describe the synthesis of a corrorin-type dihydrosapphyrin isomer (**1**), to which we put a trivial name "dihydrosapphyrinarin", its ring-contracted rearrangement to the pyrrolyl norrole (**2**), its Zn^{2+} complex (**3**), and succeeding ring expansion to the terpyrrole-containing isosmaragdyrin[10] analogue (**4**). The unprecedented pyrrole transformation chemistry is illustrated.

Chart 1. Representative Structures of Porphyrin, Corrole, Sapphyrin, Smaragdyrin, Isosmaragdyrin, and Their Pyrrole-Mislinked Isomers



At first, we tried the cyclization of a pentapyrrane (**P_5**) with two terminal β-linked pyrroles, aiming to prepare the doubly N-confused sapphyrin (**N_2CS**)[11] bearing two confused pyrroles in a bipyrrole moiety (Scheme 1). However, contrary to our expectations, the cyclization reaction proceeded in a $\beta,\alpha-\alpha,\beta$ mode instead of the $\beta',\alpha-\alpha,\beta'$ one and afforded a dihydrosapphyrinarin (**1**) with an sp^3 *meso*-carbon, similar to the cyclization of the doubly N-confused bilane to corrorin.[6b]

As inferred from the transformation of corrorin to oxyindolophyrin,[6a] the bipyrrole moiety with the $\beta,\alpha-\alpha,\beta$ linkage

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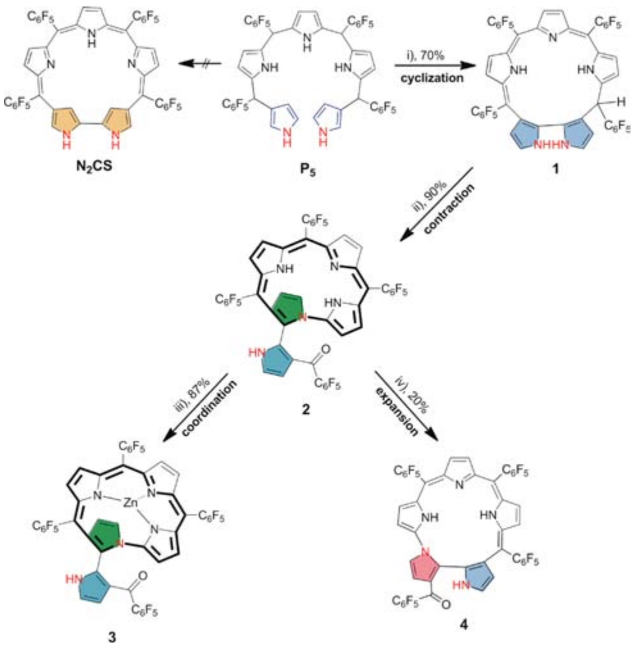
Scheme 1. Syntheses of 1−4[a]



[a]Conditions: (i) DDQ, CH_2Cl_2; (ii) Et_3N, CH_3CN, air; (iii) $Zn(OAc)_2{\cdot}2H_2O$, MeOH; (iv) DDQ, CH_2Cl_2.

in **1** was rather reactive, and the pentapyrrolic macrocycle **1** readily underwent a ring contraction reaction to afford a high yield of tetrapyrrole macrocycle, pyrrolyl norrole (**2**, Scheme 1). Surprisingly, **2** further underwent a ring expansion reaction to afford a novel pentapyrrolic macrocycle (**4**), in which two confused pyrroles are linked in an unprecedented N,$\alpha-\alpha,\beta$ mode. It has only three *meso* carbons in the conjugated pathway and a terpyrrole, and thus it can be described as an isosmaragdyrin[10] analogue.

To be more specific, the precursor, doubly terminal β-linked pentapyrrane ($\mathbf{P_5}$), was synthesized from tripyrrane and β-pyrrole carbinol, and then oxidized with 3.3 equiv of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to afford **1** in 70% yield. **1** was stable in the air, but upon further addition of DDQ, decomposed gradually. Interestingly, when **1** was treated with Et_3N in acetonitrile, it underwent ring contraction to afford a norrole derivative **2** with an appended aroylpyrrole ring in 90% yield. The reaction solvent is vital for this transformation: the yield was decreased to 30% in CH_2Cl_2 and almost no desired product was obtained in the alcoholic or alkane solvents. In the next step, when **2** was treated with $Zn(OAc)_2{\cdot}2H_2O$ in methanol, Zn^{2+} complexation was achieved with the change of solution color from blue to green. The resulting Zn^{2+} complex **3** was separated on a silica gel column as a green solid in 87% yield. Furthermore, contrary to the ring contraction from **1** to **2**, the norrole **2** underwent a ring expansion reaction to afford a novel pentapyrrolic isosmaragdyrin analogue **4** in 20% yield by treatment with 1 equiv of DDQ in CH_2Cl_2.

The structures of compounds **1**−**4** were characterized by single crystal X-ray diffraction analyses.[12] The crystal of **1** (Figure 1a,c) demonstrated a nonplanar pentapyrrolic macrocycle with a directly linked bipyrrole in a unique $\beta,\alpha-\alpha,\beta$ mode and an sp^3 *meso*-C atom, and the internal ring pathway contains a minimum of 17 atoms. Within the molecule, the regular pyrrole rings A and B are almost coplanar, and the C, D, and E pyrroles are tilted from this plane with dihedral angles of 26.4°, 35.3°, and 89.5°, respectively. Within the macrocycle, N4 is hydrogen bonded to H3 and H5 with N4···N3 and N4···N5 distances of 2.71 and 2.65 Å, respectively.

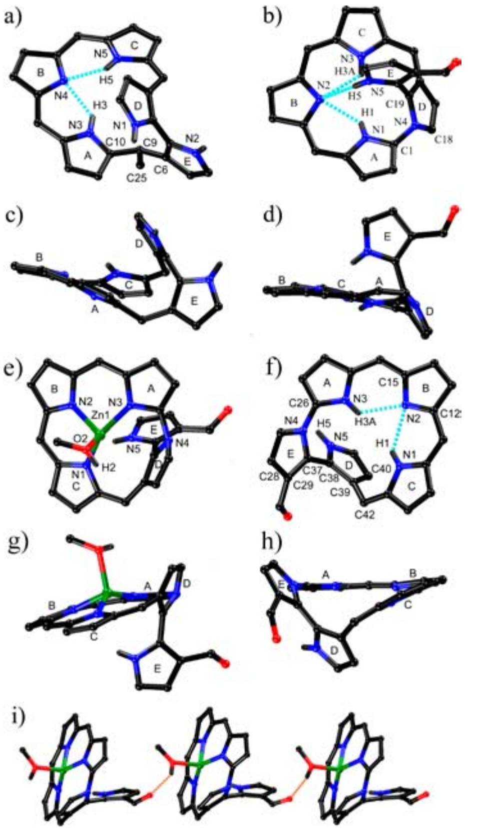


Figure 1. Perspective and side views of molecular structures of **1** (a,c), **2** (b,d), **3** (e,g), and **4** (f,h), and the 1D chain (i) assembled by intermolecular hydrogen bonds in crystal **3**. C_6F_5 groups and the hydrogens attached to carbons are omitted for clarity.

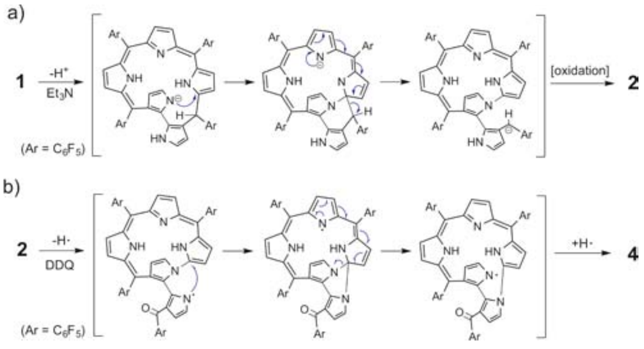
The crystal structure of **2** (Figure 1b,d) revealed that the pentapyrrolic macrocycle **1** has been contracted to a tetrapyrrolic macrocycle—a norrole derivative with an appended pyrrolic ring at the C19 position—and the internal ring pathway contains a minimum of 15 atoms. The regular B and C pyrrole rings are almost coplanar, and the pyrroles A and D are tilted from this plane with dihedral angles of 19.3° and 55.3°, respectively. These values are significantly larger than those (6.7° and 34.1°) observed for C19-unsubstituted norrole,[5a] indicating the severe distortion of the molecule due to the steric hindrance associated with the appended pyrrole E. As expected, ring E is almost perpendicular to D with a dihedral angle of 86.5°. Within the macrocycle, N2 is hydrogen bonded to H1, H3A, and H5.

Complex **3** (Figure 1e,g) also has a nonplanar structure. **2** coordinates as a dianionic, tridentate ligand, with Zn1−N1, Zn−N2, and Zn−N3 bond lengths of 1.954(5), 1.947(4), and 1.951(4) Å, respectively. The Zn center further coordinates with a methanol molecule, with Zn1−O2 bond length of 2.044(4) Å. The pyrroles C and D are tilted from the plane composed of rings A and B with the dihedral angles of 12.7°, and 59.7°, respectively. The coordination moieties are assembled by intermolecular hydrogen bonds between the axially coordinated methanol and the carbonyl moieties to form a 1D chain (Figure 1i).

In the crystal structure of **4** (Figure 1f,h), the appended pyrrole in **2** has been merged into the macrocycle to afford a pentapyrrolic macrocycle, and the internal ring pathway contains a minimum of 16 atoms (Scheme 1). The pyrroles D and E are linked directly in an unprecedented *β*,*α*−*α*,N mode. The macrocycle framework is also severely distorted from a planar structure. Namely, the regular pyrroles A and B are almost coplanar, and C, D, and E pyrroles are tilted from this plane with dihedral angles of 23.2°, 54.8°, and 57.6°, respectively. Rings C and E are also tilted from D with large dihedral angles of 71.9° and 53.1°, respectively. Similar to **1** and **2**, multiple intramolecular hydrogen bonds are also observed.

The details of the formation mechanism for **2** and **4** are yet unknown, but the above crystal structures strongly suggest intramolecular rearrangements among the three pyrrole rings A, D, and E, which are adjacent to each other (Figure 1). For **1**, ring D is located above ring A, and the distance between N1 (ring D) and C10 (ring A) is only 3.61 Å. Similarly, for **2**, the distance between N5 (ring E) and C1 (ring A) is only 3.37 Å. Thus, we think the deprotonation of N1 in **1** by Et_3N and N5 in **2** in the presence of DDQ, both of which afforded the reactive nitrogen species, could trigger the peculiar rearrangements, respectively (Scheme 2). It is noteworthy that the rearrangement from **2** to **4** is an isomerization rather than an oxidation reaction even though DDQ was used.

Scheme 2. Plausible Mechanism for the Formation of 2 (a) and 4 (b)



The facile formation of **1** instead of $\mathbf{N_2CS}$ from the precursor $\mathbf{P_5}$ was inferred from the comparison of relative energies of **1** and the dihydrogenated $\mathbf{N_2CS}$ (Figures 2 and S12, Supporting Information). The density functional theory (DFT) calculations[13] on the reduced form of $\mathbf{N_2CS}$ tautomers (**1a**, 79.4 kJ/mol; **1b**, 62.0 kJ/mol) have demonstrated much higher energies than **1** (0.0 kJ/mol). These results indicate that the incorporation of *α*,*β*′-linked pyrroles in this macrocyclic system is unfavorable, and hence the partially oxidized compound **1** was obtained in the cyclization reaction. On the other hand, the energy of **4** (−31.9 kJ/mol) is much lower than that of **2** (0.0 kJ/mol), which indicates that the ring expansion reaction is energetically favorable, being consistent with the experimental results.

The absorption spectra of **1**−**4** exhibit broad Soret-like and Q-like bands with comparable intensities (Figure 3a), which indicates the nonaromaticity of **1**−**4**.[14] It is noteworthy that **1**, **2**, and **4** exhibit extremely weak fluorescence in CH_2Cl_2, with the quantum yields of 0.22%, 0.16%, and 0.31%, respectively.[15] In contrast, **3** exhibits a much stronger emission peak at 741 nm (Figure 3b) with the quantum yield of 9.9% in CH_2Cl_2.[15]

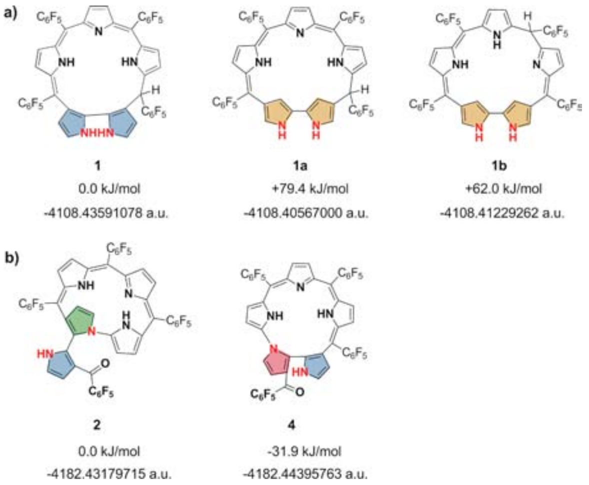


Figure 2. Relative energies (kJ/mol) and computed self-consistent field energies (a.u.) for (a) the possible isomers of **1** and (b) **2** and **4**.

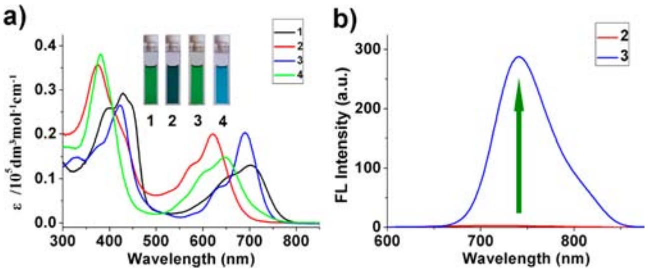


Figure 3. (a) UV−vis spectra and photographs showing the solution colors of **1**−**4** in CH_2Cl_2. (b) Fluorescence spectra (λ_{ex} = 422 nm) of **2** and **3** (10 *μ*M) in CH_2Cl_2.

Consistent to these data, the addition of Zn^{2+} to the methanol solution of **2** induced drastic absorption spectral changes, and 31-fold fluorescence enhancement at 736 nm (Figure S13, Supporting Information), which may be ascribed to a chelation-enhanced fluorescence (CHEF) mechanism.[16] The diminished fluorescence property of norrole skeleton[5a] in distorted **2** could be recovered by fixing the molecular structure with metal chelation. This observation indicated that **2** would be developed as a prototype of Zn^{2+} probe with NIR emission, which is now under research in our laboratory.

In summary, we have sequentially synthesized three types of novel porphyrinoids **1**, **2**, and **4**, which contain unique *β*,*α*−*α*,*β*, *α*,*α*−N,*β*, and N,*α*−*α*,*β*, bipyrrole linkages in the 17-, 15-, and 16-membered macrocyclic frameworks, respectively. The macrocycles **1**, **2**, and **4** exhibit extremely weak fluorescence. In contrast, **3** exhibits a much stronger emission peak at 741 nm, and thus **2** may find applications in Zn^{2+} probing. The present results do not merely add examples to the ring-size-changing reaction in porphyrinoids[17] but suggest the validity of the confusion approach strategy. Because of the innumerable combinations of confused and regular pyrroles, we believe hitherto novel molecules with unprecedented frameworks and interesting functions could be discovered by the confusion approach strategy.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic procedures and complete experimental details; crystallographic details (CIF) for **1**−**4**; spectroscopic and analytical data (UV−vis, FL, NMR); details on DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(12) CCDC 950263−950266 (**1**−**4**) contain 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/date_request/cif.

(13) All the calculations were achieved with Gaussian09 program package at the B3LYP/6-31G* level. See Supporting Information for calculation details.

(14) More detailed descriptions on the aromaticity of **1**−**4** are included in the Supporting Information.

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