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Expanded Porphyrins: More Confusion All the Time**

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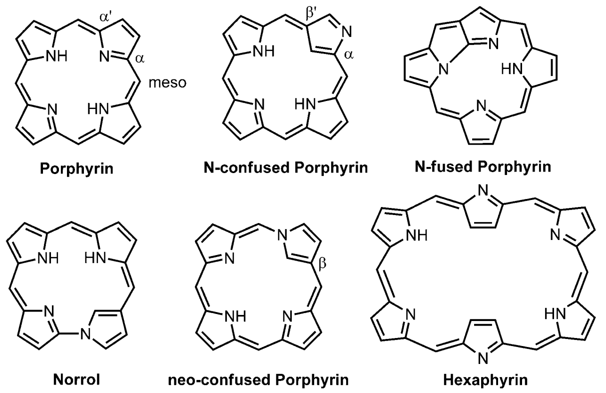
Macrocyclic compounds widely occur in nature. For example, porphyrins (Figure 1) are known as "pigments of life", showing interesting biochemical and optoelectronic functions. In recent years, intensive attention has been paid to the development of novel porphyrin analogues (porphyrinoids) with advanced novel structures, intriguing reactivity, and unique properties that may be unrealizable from normal porphyrins, such as tunable aromaticity and multi-metal coordination.[1] In this respect, changing the linking modes between the pyrrole units and expanding the size of the conjugated ring have been demonstrated to be two promising approaches.



Porphyrin

N-confused Porphyrin

N-fused Porphyrin

Norrol

neo-confused Porphyrin

Hexaphyrin

Figure 1. Chemical structures of porphyrin and representative analogues.

Porphyrin contains four pyrroles that are interconnected at the α positions through the meso carbon atoms. By changing the linking modes, N-confused porphyrin (Figure 1), which contains an α,β′-linked (confused) pyrrole, was first designed and synthesized independently by the groups of Furuta and Latos-Grażyński in 1994.[2–4] Compared with the α,α′-linked pyrroles in normal porphyrins, the confused pyrrole exhibits much higher reactivity.[5] For example, it can undergo ring-fusion reactions to afford N-fused porphyrins.[5] In 2011, Furuta and co-workers reported the first example of a tetrapyrrolic macrocycle containing a C−N-linked bipyrrole unit, which was named norrole.[6] In the same year, Lash et al. reported neo-confused porphyrin,[7] which also contains an N-linked pyrrole. It can be regarded as another important new class of porphyrin isomers.[7]

Expanding the macrocycle size of porphyrins is another important approach for developing novel porphyrinoids, such as hexaphyrin. Through ring size expansion, the flexibility of the macrocycle and the space of the central cavity will be increased. Thus, expanded porphyrins exhibit diverse conformations and can coordinate more than one metal atom at the same time. By varying the conformation and the oxidation/reduction state, both Hückel and Möbius aromaticity can be realized in expanded porphyrin systems.[8]

Considering the aforementioned background, it was postulated that more unique structures could be obtained by combining the "confusion" and "expansion" approaches. In this respect, Xie and co-workers developed a new synthetic strategy that involves the direct linking of two confused pyrroles (Figure 2).[9,10] Two confused pyrroles were placed at the terminal positions of pentapyrrane. Subsequent oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded novel porphyrinoid **1**, which contains two pyrrolic units directly linked in the β,α-α,β mode. This compound was

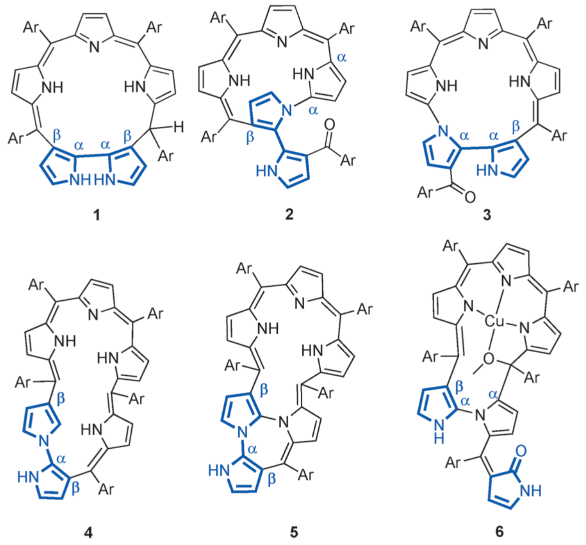


Figure 2. Representative structures of expanded porphyrinoids with directly linked confused pyrroles highlighted in blue.[9,10] Ar = pentafluorophenyl.

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named dihydrosapphyrin[9] and displayed a highly twisted conformation owing to the presence of an unconventionally linked bipyrrole unit and an sp^3-hybridized meso carbon atom. Interestingly, when porphyrinoid **1** was treated with Et_3N, it underwent a macrocycle contraction reaction to afford pyrrolyl norrole **2** in an impressive yield of 90%. Subsequent treatment with DDQ induced a ring expansion reaction with merging of the appended pyrrolyl moiety into the pentapyrrolic macrocycle to afford **3**. The formation and cleavage of interpyrrolic C—N bonds obviously plays an important role in these reactions. Compound **3** has a pentapyrrolic macrocycle framework with three meso carbon atoms, and thus it can be regarded as an isosmaragdyrin. DFT calculations revealed that the relative energy of **3** is much lower than that of **2**, which may account for the fact that **2** can be readily converted into **3**.

Building on this successful work, Xie and co-workers continued to work on the cyclization of a hexaphyrrane containing two terminal confused pyrroles, which afforded neo-confused hexaphyin **4**.[10] It contains a unique β,*N*-α,β-linked bipyrrole unit and displays a highly twisted conformation and high reactivity. Because of the twisted conformation, a very short interpyrrolic C···N distance of 3.102 Å was observed in the crystal structure, which may facilitate the formation of a C—N bond between these two atoms. In consistency with this hypothesis, when **4** was further oxidized with DDQ, it underwent a unique ring-fusion reaction to afford neo-fused hexaphyrin **5** with an unprecedented 5,5,5,7-tetracyclic structure through generation of a new C—N bond. Hexaphyrin **5** contains a highly distorted seven-membered C_5N_2 ring, and thus it may be highly reactive. Indeed, coordination of **5** to a Cu^{2+} ion triggered a ring-opening reaction that afforded pentaphyrin **6**. Similar to the observations for **1**–**3**, the formation and cleavage of interpyrrolic C—N bonds also plays an important role in the unique ring-fusion and ring-opening reactions from **4** to **6**.

As described above, all compounds **1** to **6** are highly twisted. For example, pyrrolyl norrole **2** is severely distorted because of the steric hindrance associated with the appended pyrrolyl unit, and thus it is nonaromatic, even though norrole is aromatic.[6] When **2** is coordinated to a Zn^{2+} ion to afford Zn-**2**, the rigidity of the molecule will be significantly enhanced by the chelation, resulting in drastically enhanced fluorescence at 736 nm (Figure 3 a). Similar to **2**, neo-confused hexaphyrin **4** also shows relatively weak fluorescence at approximately 900 nm because of its twisted and flexible structure, but the rigidity is dramatically improved in neo-fused hexaphyrin **5** owing to the presence of an extra seven-membered ring. Therefore, hexaphyrin **5** shows much stronger fluorescence than **4** (Figure 3 b).

Compared with α,α′-linked pyrroles in porphyrins, the confused pyrroles are much more reactive. For the convenience of synthesis, the confused pyrrole units are usually separated by regular ones. In contrast, Xie et al. developed a convenient and effective strategy for the synthesis of novel confused porphyrinoids by oxidative ring-closure reactions of linear oligopyrranes containing two terminal confused pyrroles.[9,10] This approach was demonstrated to be effective for synthesizing the first examples of expanded porphyrinoids with two directly linked confused pyrroles, which showed unique cooperative reactivity; unique macrocycle contraction, expansion, fusion, and opening reactions were thus successfully performed under mild reaction conditions. Various novel porphyrinoids with unique bipyrrole linking modes (β,α-α,β, α,α-*N*,β, *N*,α-α,β, β,*N*-α,β, β,*N*-α,β, and β,α-*N*,α) were then synthesized. The important roles of interpyrrolic C—N bonds in the macrocycle transformations have thus been demonstrated.

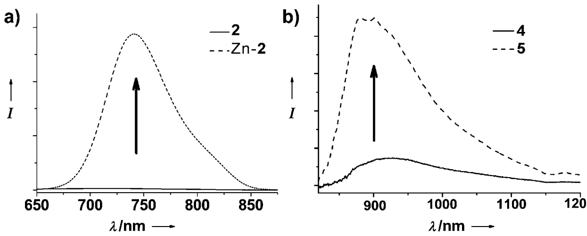

Figure 3. Enhancement of the fluorescence emission of **2** and **4** upon their conversion into Zn-**2** and **5**, respectively.

In summary, oxidative ring-closure reactions of oligopyrranes containing two terminal confused pyrroles are effective methods for the synthesis of porphyrinoids with two directly linked confused pyrroles, which show cooperative reactivity, and thus constitute a new method for the synthesis of novel porphyrinoids with unconventional pyrrole linking modes and unique properties.

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