FEATURE ARTICLE

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Confusion, inversion, and creation—a new spring from porphyrin chemistry

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This article mainly deals with the recent serendipity of novel porphyrin analogs such as N-confused porphyrin. The unique property of this ligand allows the formation of a variety of metal complexes. The important aspect of dynamic flipping (*inversion*), induced either by *confusion* or *expansion* of the macrocyclic core, that leads to the generation of new porphyrinoids, is emphasized. This review concludes with the recent progress on expanded porphyrins bearing *confused*, *inverted*, and *fused* pyrrole rings.

Hiroyuki Furuta was born in Fukuoka, in 1956. He received his PhD degree from Kyoto University in 1986 on the photo-induced electron transfer reaction of porphyrins under the direction of Professor Kazuhiro Maruyama. In 1986, he joined the group of Dr Hiroshi Yanagawa at the Mitsubishi-Kasei Institute of Life Science at Machida and worked on the subject of origin of life. In 1989, he moved to Professor Jonathan L. Sessler's lab at the University of Texas, Austin as a postdoctoral fellow. In 1992, he started an academic carrier at the Faculty of Engineering of Oita University as an associate professor. In 1997, he moved to the Department of Chemistry of Kyoto University as an associate professor. In 1999, he was selected as a researcher in Precursory Research for Embryonic Science and Technology (PRESTO), Japan Science and Technology Corporation (JST). His research interests cover synthesis of novel porphyrinoids for functional dyes, metal coordination chemistry for supramolecular architectures, and chemical evolution.

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Introduction

Porphyrin is a widely studied functional pigment that can coordinate a variety of metals with four pyrrolic nitrogens in a square planar arrangement in the core. What would happen or could be observed if the porphyrin core is modified? How are their properties different from the standard porphyrins? With a view to answering such questions, modification of porphyrin core skeleton and/or synthesis of new porphyrin analogs such as expanded, contracted, and isomeric porphyrins, have been actively pursued to develop a new realm of porphyrinoid chemistry.[1,2]

The study of artificial porphyrin analogs started in 1960s but the flourishing of research on this subject in recent years has been due largely to the availability of modern instruments such as high resolution NMR and, especially, single crystal X-ray diffractometers, which are indispensable for ambiguous structural determination. In 1986, the first porphyrin isomer, porphycene ([18]porphyrin-(2.0.2.0)) that differs in the pyrrole-linking carbon chain from that of the normal one ([18]porphyrin-(1.1.1.1)) was synthesized by Vogel *et al*.[3,4] Since then, the other configurational isomers containing the same $C_{20}H_{14}N_4$ composition, such as corrphycene ([18]porphyrin-(2.1.0.1)),[5] hemiporphycene ([18]porphyrin-(2.1.1.0)),[6,7] isoporphycene ([18]porphyrin-(3.0.1.0))[8] and so on, have been reported. In 1994, Latos-Grażyński *et al*. and ourselves independently isolated a completely different isomer of [18]-(1.1.1.1) type, N-confused porphyrin (NCP),[9–13] in which one of the pyrrole rings was connected to *meso*-carbons at α and β' positions, from the reaction mixture of pyrrole and arylaldehyde condensation. This isomer, formally classified as a *carbaporphyrin*, showed characteristic properties owing to the *confused* pyrrole ring that possessed an inner core carbon and a peripheral nitrogen in the skeleton (Chart 1).

On the other hand, increasing attention has been paid to a class of porphyrin analogs with different core sizes, namely, contracted and expanded porphyrins. In the natural system, vitamin B_{12} is known to have a contracted porphyrin framework which is known as *corrin*.[14] In 1964, Johnson *et al*. synthesized the first contracted porphyrin with an 18 π-electron system, corrole, wherein one of the *meso*-carbons was missing in the skeleton, by the cyclization of a tetrapyrrolic precursor.[15] Efficient one-pot syntheses of *meso*-substituted corroles were reported recently.[16,17] In 1966, Woodward reported the first example of an expanded porphyrin with a 22 π-electron system, sapphyrin, which contained five pyrrole rings and four *meso*-carbons.[18] The higher homolog with all methine-bridges, pentaphyrin, was reported by Gossauer in 1983 and shown to sustain a 22 π-aromatic periphery (Chart 2).[19] Since then, various expanded porphyrins have been synthesized and

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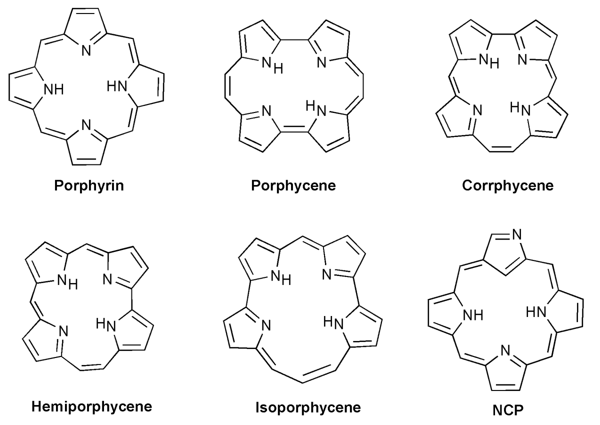


Chart 1 Porphyrin and its isomers.

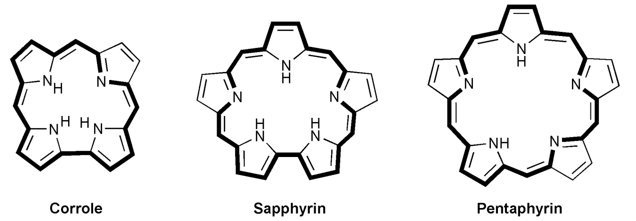


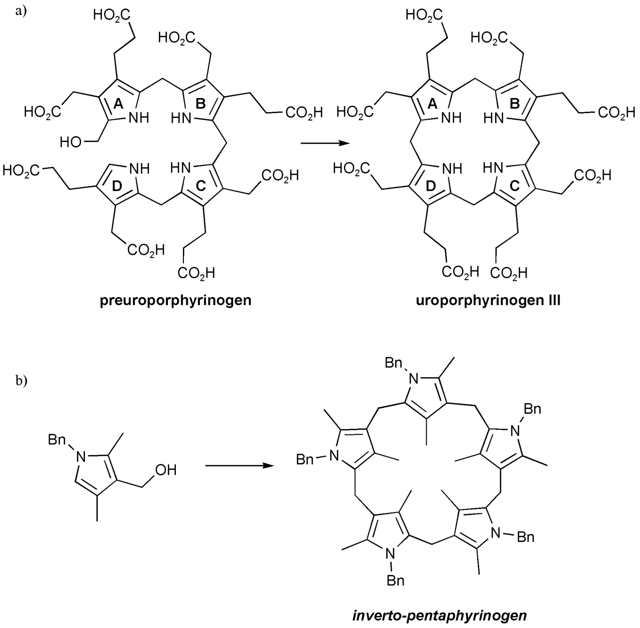
Chart 2 Contracted and expanded porphyrins. Aromatic circuits are represented in bold lines.

investigated for medical applications such as anion recognition,[20,21] magnetic resonance imaging (MRI),[22] photodynamic therapy (PDT),[23] and so on. Recently, we have isolated a series of *meso*-aryl expanded porphyrins and succeeded in determining their structures by X-ray analyses up to nonaphyrin from the one-pot pyrrole–arylaldehyde condensation.[24,25] In these porphyrinoids, the dynamic flipping of a pyrrole ring (*inversion*, defined in the following section) that is induced by either *confusion* or *expansion* of macrocycles gives rise to unique properties that have never been observed for the porphyrins.

In this article, we wish to describe recent progress of porphyrinoid chemistry, especially focusing on our results. At first, characteristic properties of N-confused porphyrin such as NH-tautomerism, inside and outside metal coordination chemistry are described. Second, new generations of *confused* porphyrin analogs and the transformation of the *confused* unit are introduced. Third, *meso*-aryl expanded porphyrins and their correlation with *inversion* and *confusion* are discussed. Finally, the important role of inversion for the creation of novel porphyrinoids with *fused* ring systems is emphasized.

Confusion and *inversion*

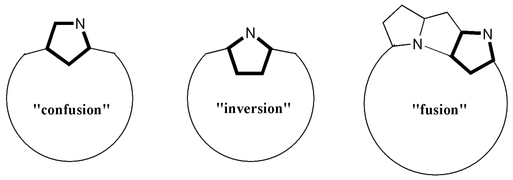
Before describing the N-confused porphyrin chemistry in detail, we wish to draw attention to the term *inversion* in order to avoid any misreading. At present, several names can be seen in the literature to represent the macrocycle containing the pyrrole unit bearing α- and β′-linkage: carbaporphyrin, inverted porphyrin, N-confused porphyrin, mutant porphyrin, 2-aza-21-carbaporphyrin, *etc.*[9–13] Among these terms, *inverted* or *inversion* has been used in the ring rearrangement process of the terminal D-ring of preuroporphyrinogen to uroporphyrinogen III, where the position of acetic and propionic acids are exchanged, in the biotic heme synthesis (Scheme 1a).[26,27] In 1989, a completely different meaning of *inversion*, namely, the α-, β′-linkage of the porphyrinoid, was introduced by Franck *et al.*[28,29] They synthesized a fully α,β′-linked pentaphyrinogen, *inverto-pentaphyrinogen*, but failed to dehydrogenate it to the corresponding conjugated porphyrinoid (Scheme 1b). The third usage of the term *inversion* was as an outward pointing



Scheme 1 Syntheses of (a) uroporphyrinogen III and (b) *inverto-pentaphyrinogen.*

arrangement of a pyrrole ring that was frequently observed in expanded porphyrins.[21,24,25]

Here, we define the terms *confusion*, *inversion*, and *fusion* as used in this article. In the normal porphyrin framework, α and α′ linkage is ordinary. *Confusion* is defined as a linkage at the α and β (β′) positions of pyrroles or other hetero-pentacycles (Scheme 2). *Inversion* means the pyrrole and other pentacycles' ring flipping and *inverted* is a state of pyrrole pointing outward. *Fusion* is used for the formation of a tripentacyclic ring by connection of a pyrrole ring to a neighbouring *inverted* pyrrole with its nitrogen.

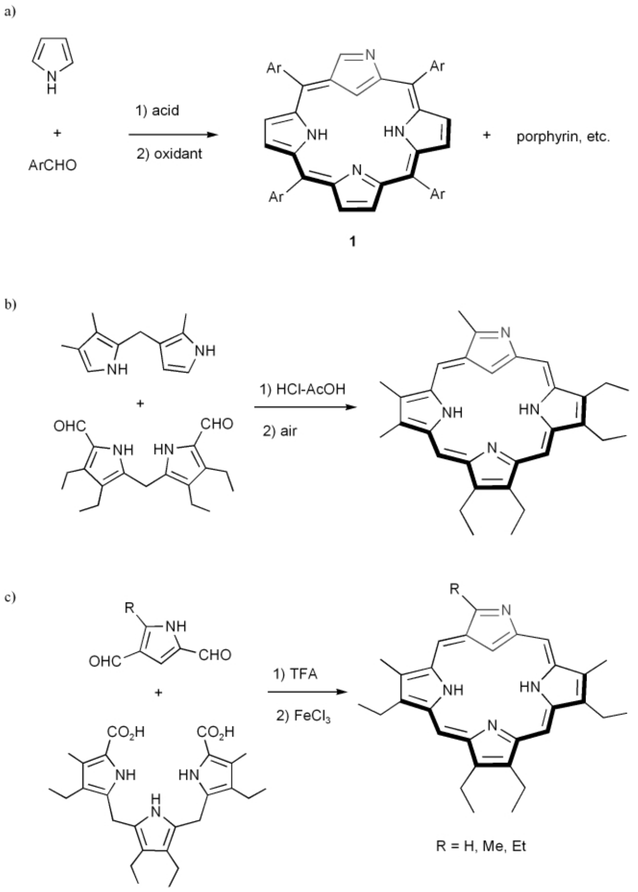


Scheme 2 Schematic representation of *confusion*, *inversion*, and *fusion* in pyrrolic systems.

N-confused porphyrin

Meso-substituted N-confused porphyrin (NCP) was synthesized by the Rothemund type reaction,[30] namely, acid catalysed pyrrole–aldehyde condensation, with concurrent formation of normal porphyrin. Although the isolated yield reported in 1994 was low (N-confused tetraphenylporphyrin (NCTPP, **1**): 5–7%[9] and N-confused tetratolylporphyrin (NCTTP, **1′**): 4%[10]), Lindsey *et al.* have improved the reaction yield up to 39%.[13,31,32] On the other hand, *meso*-free type forms of NCP were prepared in a stepwise manner using MacDonald-type [2 + 2] and [3 + 1] condensation by Dolphin's[33] and Lash's[34] groups, respectively (Scheme 3).

NCP analogs containing hetero-atoms such as O, S, and Se have also been synthesized by the groups of Lee,[35–39] Latos-Grażyński,[40–42] and Chandrashekar *et al.*[43] Furthermore, Lash and co-workers reported syntheses of a series of CNNN- and CNCN-core porphyrins including 'true' carbaporphyrins, which contain a cyclopentadienyl unit in the macrocycle.[44–48] These compounds could serve as good references for the study of NCP chemistry.



Scheme 3 Syntheses of N-confused porphyrins from (a) Rothemund type and MacDonald type (b) [2 + 2] and (c) [3 + 1] condensation.

In contrast to the planar *meso*-tetraphenylporphyrin (TPP), the core plane of NCTPP was distorted and the *confused* pyrrole ring was tilted 26.9° in the solid state,[9] probably due to the steric hindrance in the core (Fig. 1a). Actually, when a sizeable nitro group was introduced at the inner carbon, the *confused* pyrrole ring of NCP (**1′-NO$_2$**)[49] was more canted to an angle of 42.4° (Fig. 1b). The structures revealed by X-ray analyses were also in line with the theoretical calculations for the NCP core.[50–52]

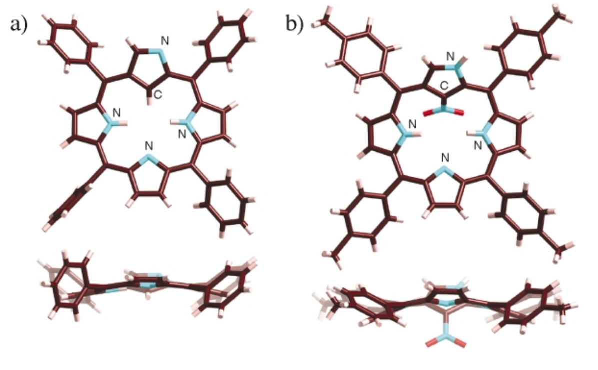
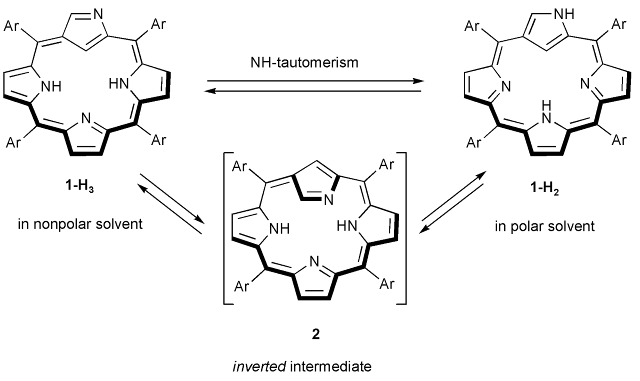


Fig. 1 X-ray structures of (a) NCTPP (**1**) and (b) NO$_2$ substituted NCTTP (**1′-NO$_2$**).

NH-tautomerism of N-confused porphyrin

Due to the presence of the core and the peripheral nitrogens, NH-tautomerism of N-confused porphyrin (NCP) can take place between inner and outer nitrogens and the tautomer distribution may change with solvent.[53,54] In nonpolar solvents like $CHCl_3$, an inner 3H tautomer (**1-H$_3$**) of an 18π aromatic system predominates, whereas an inner 2H tautomer (**1-H$_2$**) predominates in polar, hydrogen-bonding accepting solvents like DMF (Scheme 4). As a result, the colors of NCTPP solutions differ greatly, red in $CHCl_3$ and green in DMF. The two tautomers also differ greatly in structure, absorption spectra, and aromaticity. The X-ray single crystal analysis of **1-H$_2$** (obtained from DMF/MeOH) revealed that the molecule was fairly flat and the *confused* pyrrole ring was tilted only 4.7° reflecting lesser crowding in the core compared with **1-H$_3$**. In the solid state, a DMF molecule was hydrogen bonded with the outer NH of the *confused* pyrrole (Fig. 2).



Scheme 4 NH-tautomerism of NCTPP (**1**).

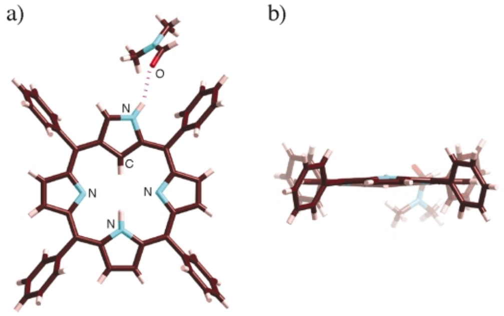


Fig. 2 X-ray structure of NCTPP inner 2H tautomer (**1-H$_2$**) and DMF molecule, (a) top view and (b) side view. Hydrogen bonding interaction is indicated by a broken line.

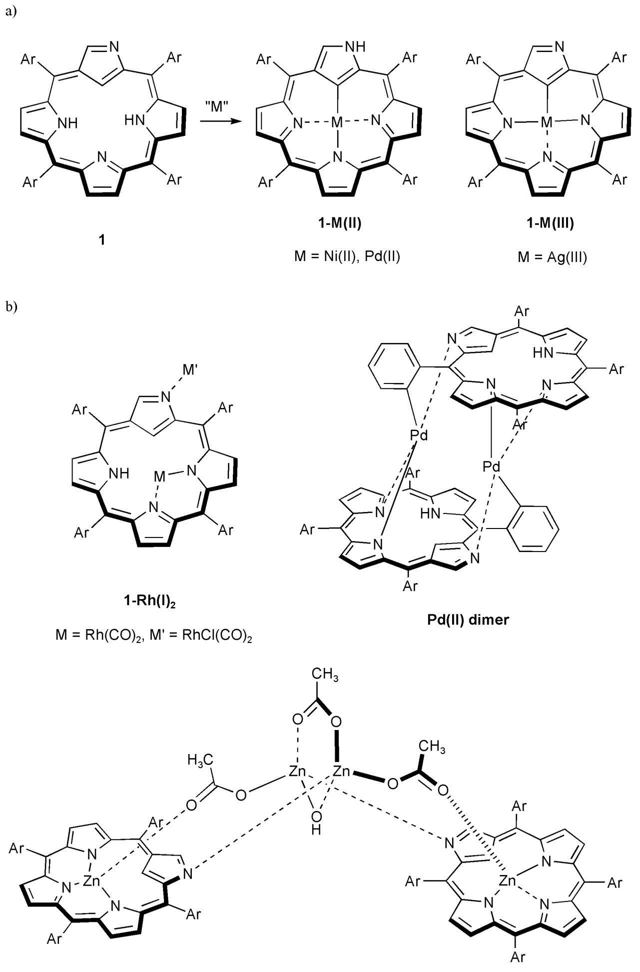
The ^1H NMR signals derived from the inner CH and NH of **1-H$_3$** in $CDCl_3$ resonate at −4.99 and −2.41 ppm, respectively. On the other hand, the corresponding signals of **1-H$_2$** in DMF-d_7 are shifted to 0.76 and 2.27 ppm, respectively, in addition to the appearance of an outer NH signal at 13.54 ppm. The downfield shifts of inner protons in DMF-d_7 is attributable to disruption of the 18π system in **1-H$_2$**. The dynamic process of NH tautomerism of NCTPP was studied by ^1H NMR saturation transfer experiments in pyridine-d_5 solution, where both the tautomers could exist in comparable amounts. Based on the large negative value of the activation entropy, the drastic conformational change in the transition state (**2**), where the *confused* pyrrole ring *inverts* to draw the 'outer' nitrogen nearer to the inner NH to receive the proton, was postulated.[53]

Related to this tautomerism, specific halide recognition by NCP at the air–water interface was investigated.[55] The iodide anion in the aqueous solution was bound by NCTPP monolayer, which was demonstrated by the absorption spectral change induced by the formation of NCTPP aggregates.

Metal coordination of N-confused porphyrin

From the structural resemblance to normal porphyrins, NCP can be expected to form complexes with a variety of metals. Actually, the unique properties of NCP metal coordination chemistry such as organometallic nature, multi-valency, inner-and outer-coordination, and so on, have been revealed progressively.

The first example of metal–carbon bond in the NCP core has been shown by Latos-Grażyński *et al*. with a divalent Ni(II) to form a tetracoordinated planar complex (**1-Ni(II)**) similar to normal porphyrins.[10] Pd(II), the same d^8 configuration metal, also gave a planar complex (**1-Pd(II)**).[56] Here, NCP served as a dianionic ligand.[34,57–60] The trianionic property of the NCP ligand, on the other hand, was demonstrated with d^8 Ag(III) complex (**1-Ag(III)**), where the deprotonation at the peripheral nitrogen of NCP occurred concomitantly (Scheme 5a).[61] The structures of such complexes were elucidated by ^{1}H NMR and X-ray single crystal analyses (Fig. 3). The trianionic mode was also observed in a Sb(V) complex, bearing two monoanionic methoxy axial ligands.[62] Furthermore, rare stable paramagnetic d^9 organocopper(II)[63] and d^6 Fe(II) complexes were reported.[64] The latter complex was coordinated with three inner nitrogens, one axial ligand in the core, and an agostic η^2 interaction of inner C–H was suggested in the solid state.



Scheme 5 Metal coordination of NCTPP (**1**), (a) inner-coordination and (b) inner- and outer-coordination types.

The nitrogen atom at the periphery of NCP can also participate in the metal coordination to assist the formation of a supramolecular assembly. For example, a monomeric bis-Rh(I) complex (**1-Rh(I)$_2$**) with inner- and outer-N coordination was obtained from the reaction of NCP and $[Rh(CO)_2Cl]_2$.[65] Two Pd(II) metal atoms were coordinated with two NCP ligands at both outer and inner nitrogens simultaneously to form double-decker type dimers along with a monomeric inner core metallated Pd(II) complex.[56] The two Pd(II) metal atoms were coordinated in a distorted square-planar fashion, by the two inner nitrogens of NCP, and an outer nitrogen and a carbon atom of the *o*-aryl group in the counter NCP. Furthermore, a type of outer coordination was also observed in the tetranuclear Zn(II) dimer complex where the two outer Zn atoms form a 6-membered ring with a hydroxy and an acetate group and the remaining two Zn atoms were coordinated with inner three nitrogens and an acetate group (Scheme 5b, Fig. 4).[66]

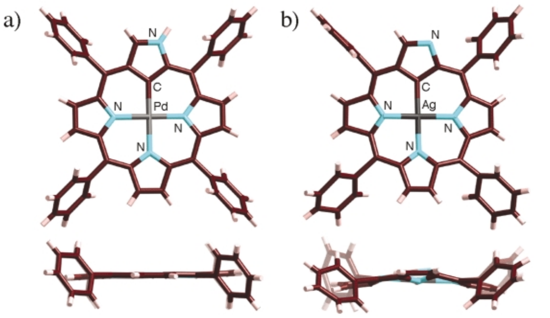


Fig. 3 X-ray structures of NCP metal complexes, (a) Pd(II) complex (**1-Pd(II)**) and (b) Ag(III) complex (**1-Ag(III)**).

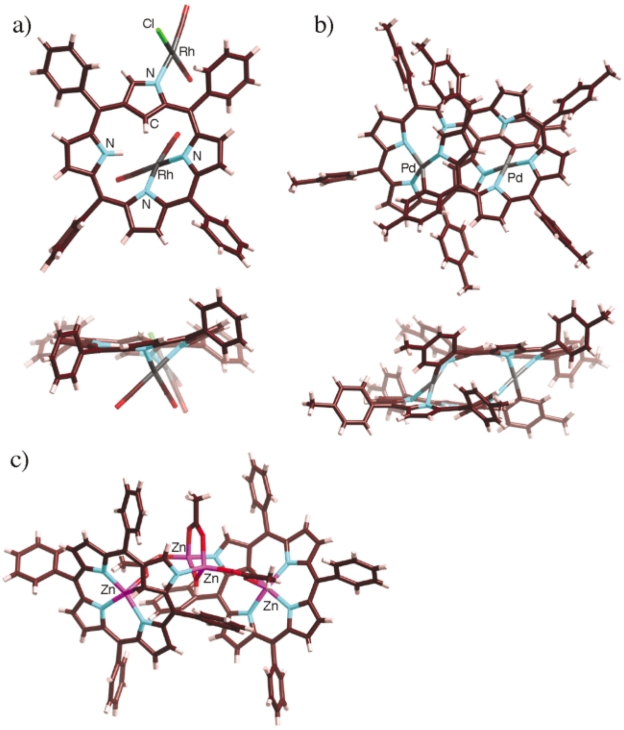
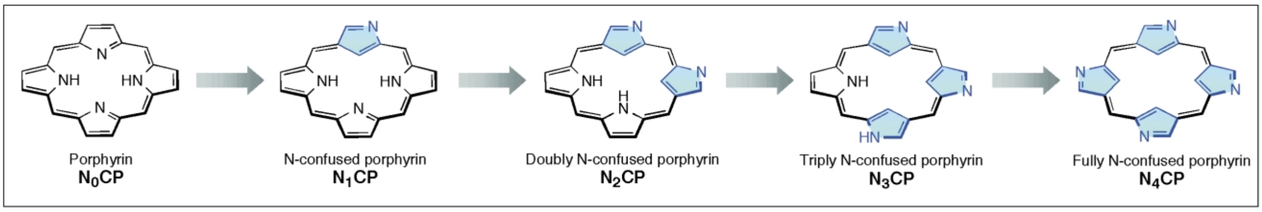


Fig. 4 X-ray structures of NCP multi-metal complexes, (a) bis-Rh(I) complex (**1-Rh(I)$_2$**), (b) double-decker Pd(II) dimer, and (c) tetranuclear Zn(II) dimer.

Second generation of N-confused porphyrin analogs

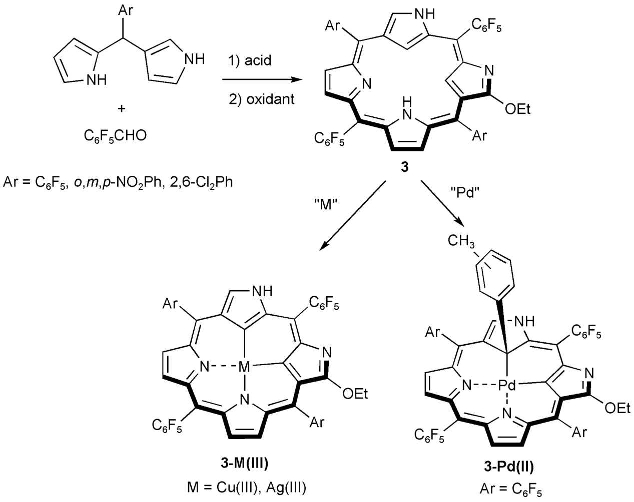
The serendipitous finding of NCP has stimulated our curiosity and tempted us to explore the *confusion chemistry* seriously. What would happen if the pyrrole rings were multiply *confused* in a single tetrapyrrolic core? Could the *confused* unit in nonconjugated systems show unique coordination chemistry? Does another mode of *confusion* exist? *etc.* In this section, new types of *confused* analogs and the derivatives, doubly N-confused porphyrin (N$_2$CP), N-confused calix[4]phyrin, corrorin and oxyindolophyrin, and tripyrrinone, are described.

Theoretically, 95 isomeric and tautomeric structures can be drawn for NCP by raising the *confusion* level (Scheme 6).



Scheme 6 Evolution of N-confused porphyrin family.

Density functional theory (DFT) calculation on all the NCP isomers and tautomers showed a stability decrease of *ca.* 18 kcal mol^{-1} per every *confusion* level.[67,68] Among such isomers, a doubly N-confused porphyrin (N_2CP) of *cis*-type (**3**), wherein two neighboring pyrrole rings were *confused*, was synthesized to reveal that it could stabilize the complexes containing Cu(III) and Ag(III) (**3-Cu(II)**, **3-Ag(III)**) (Scheme 7).[69] Interestingly, an aromatic solvent molecule was bound to the inner core carbon when **3** was treated with $Pd(OAc)_2$ to form Pd(II) complex (**3-Pd(II)**).[70] These metal complexes were stable in the air in spite of the two metal–carbon bonds in the core (Fig. 5). The electrochemistry of N_2CP, Cu(III), and Ag(III) complexes in CH_2Cl_2 solution was investigated and suggested the mediation of H_2O splitting by these complexes.[71]



Scheme 7 Syntheses of N_2CP (**3**) and its metal complexes.

To examine the *confused* system in general, the other *confused* analogues were synthesized and their metal coordination was investigated. As an example of a nonconjugated system,[72] N-confused calix[4]phyrin (**4**) wherein the sp^3 *meso*-carbon atom was present in the framework, was synthesized by the modified NCP synthesis.[73] Similar to NCP, N-confused calix[4]phyrin (**4**) behaved as a dianionic ligand to form distorted square-planar complexes with Ni(II) and Cu(II) (**4-Ni(II)**, **4-Cu(II)**) (Scheme 8, Fig. 6). The latter Cu(II) complex was the first example of an organocopper(II) complex characterized by X-ray crystallography. These results revealed that the π-conjugation system was not essential for the formation of a stable organometallic complex.

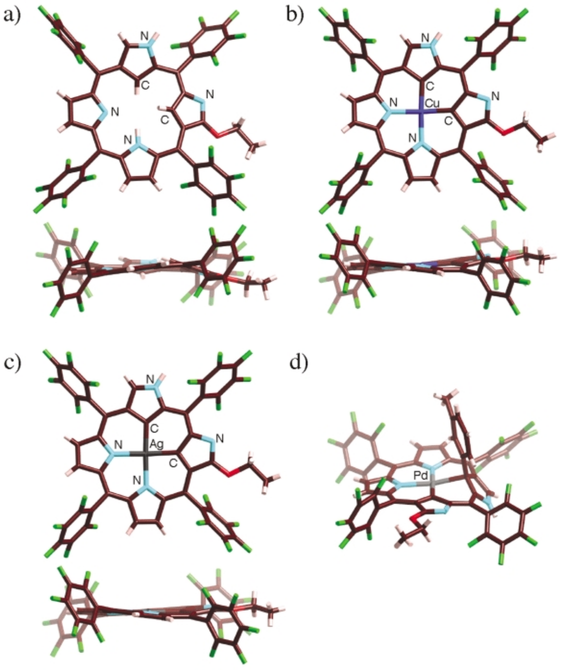
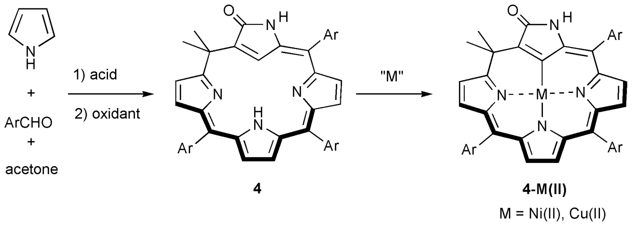


Fig. 5 X-ray structures of (a) N_2CP (**3**), (b) Cu(III) complex (**3-Cu**), (c) Ag(III) complex (**3-Ag**), and (d) Pd(II) complex (**3-Pd**).



Scheme 8 Syntheses of N-confused calix[4]phyrin (**4**) and metal complexes.

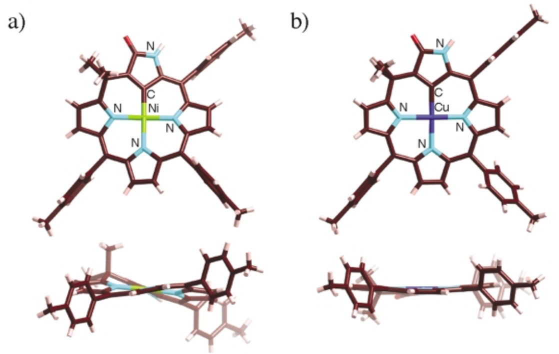
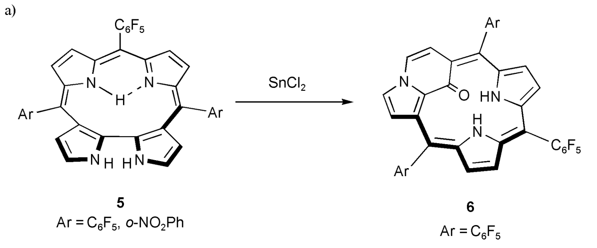


Fig. 6 X-ray structures of N-confused calix[4]phyrin metal complexes, (a) Ni(II) complex (**4-Ni(II)**), and (b) Cu(II) complex (**4-Cu(II)**).

A different type of *confused* system was observed in an N-confused corrole isomer. A novel *meso*-aryl corrole isomer (corrorin, **5**), wherein the adjacent α,β-positions of pyrrole rings were found in the linkage, was produced as the major product in the synthesis of doubly N-confused porphyrin (N_2CP, **3**).[74] Non-aromatic corrorin (**5**) was stable in air, but was found to transform into a new aromatic macrocycle (oxyindolophyrin, **6**) on treatment with $SnCl_2$ (Scheme 9). Fig. 7 shows the X-ray single crystal structures of corrorin (**5**, Ar = *o*-NO_2Ph) and oxyindolophyrin (**6**, Ar = C_6F_5). The structure of **5** was distorted from planarity largely, while **6** was rather planar. The C = O group of **6** was canted on one side and, consequently, afforded two optical isomers that could be isolated. Reflecting



Scheme 9 (a) Synthesis of oxyindolophyrin (**6**) from corrorin (**5**). (b) Zwitterionic form of oxyindolophyrin (**6**).

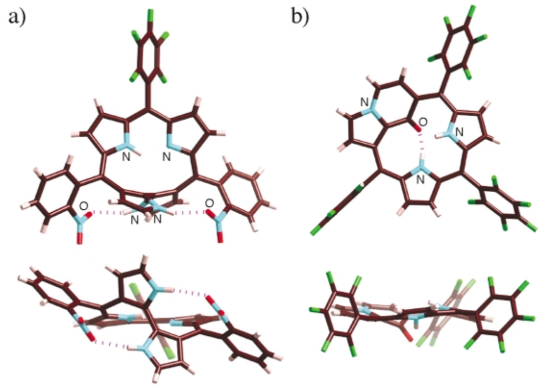


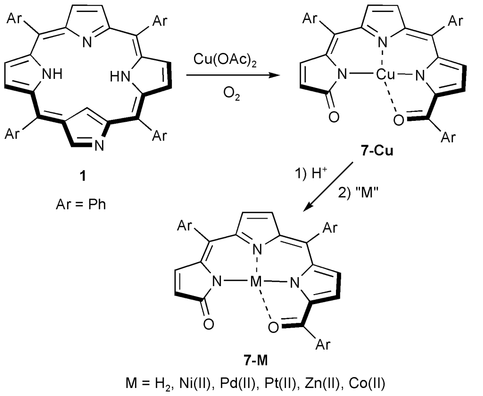
Fig. 7 X-ray structures of (a) corrorin (**5**, Ar = o-NO_2Ph) and (b) oxyindolophyrin (**6**, Ar = C_6F_5). Hydrogen bonding interactions are indicated by a broken line.

the 18π aromatic system in the zwitterionic form[48] of oxyindolophyrin, the Soret-like band was sharp as in porphyrins, whereas the optical absorption band was broad in corrorin.

The *confused* pyrrole ring of NCP was liberated under sufficiently oxidative conditions. The tetracoordinated planar Cu(II) complex of NCTPP (**1-Cu**) was synthesized from **1** and $Cu(OAc)_2$ under mild or anaerobic conditions.[63] On the other hand, under aerobic conditions, the Cu(II) complex of the aryl-substituted tripyrrinone derivative (**7-Cu**) was obtained in the reaction of NCTPP (**1**) and $Cu(OAc)_2$ in refluxing toluene, and subsequent treatment with acid afforded a free tripyrrolic ligand that could complex with a variety of transition metals (Scheme 10).[75] The X-ray structures of **7-Cu** and Pd(II) complex (**7-Pd**) were nearly planar as shown in Fig. 8.

Fusion from *inversion*

The observation of the tilting of the *confused* pyrrole ring in NCTPP (**1**)[9] and NO_2 substituted NCTTP (**1′-NO_2**)[49] (Fig. 1) drove us to a further study on the core modification with expectation of more tilting and/or flipping of the pyrrole ring. During the halogenation of **1**, we obtained a new type of porphyrinoid, N-fused porphyrin (NFP, **8**) with a *fused* tripentacyclic ring in the macrocyclic core (Fig. 9). This product should be derived as a result of ring *inversion* of the *confused* pyrrole.[76,77] More interestingly, NFP (**8**) was found to return to NCP (**1**) by *reinversion* of the pyrrole ring by treatment with base (Scheme 11). The absorption bands of NFPs reach to the near IR region around 1000 nm and such an unusual long-wavelength absorption is attractive for optical applications.



Scheme 10 Syntheses of tripyrrinone-Cu(II) (**7-Cu**) and other metal complexes (**7-M**).

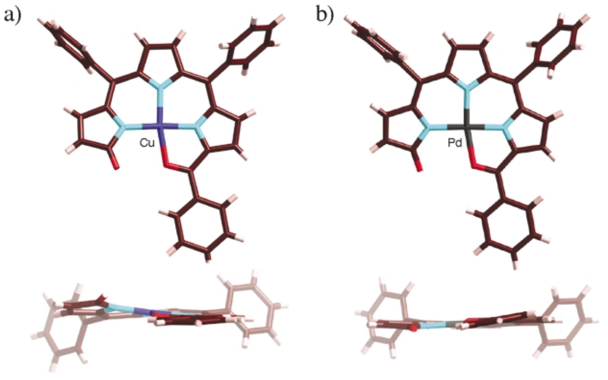


Fig. 8 X-ray structures of (a) tripyrrinone-Cu(II) (**7-Cu**) and (b) tripyrrinone-Pd(II) (**7-Pd**).

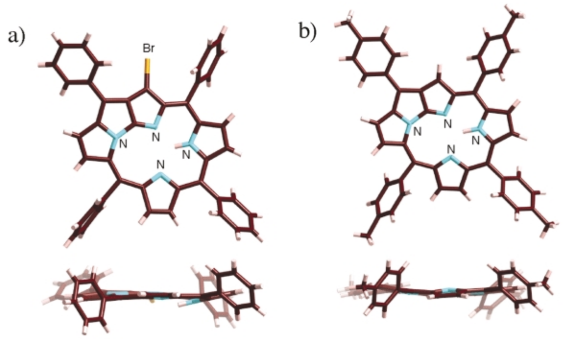
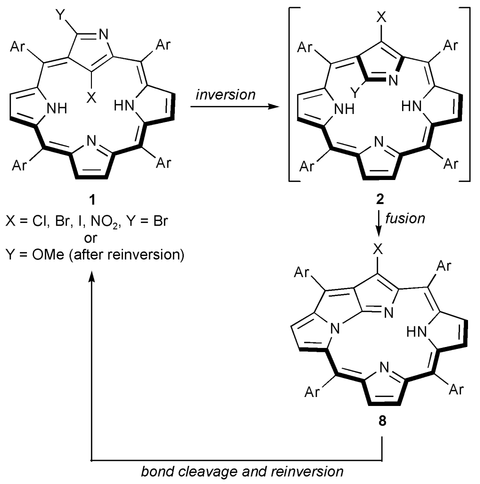


Fig. 9 X-ray structures of NFPs, (a) **8-Br** (Ar = Ph, X = Br), and (b) **8′** (Ar = tolyl, X = H).

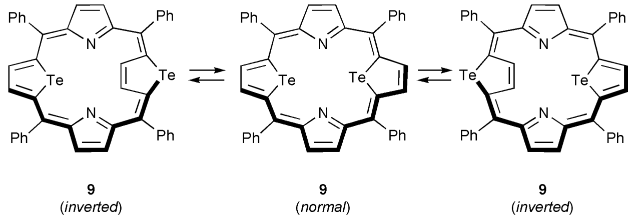


Scheme 11 Transformation between NCP (**1**) and NFP (**8**).

The reaction of NFP formation was largely affected by the substituents, both at the *meso*-position and the inner carbon. The introduction of electron withdrawing groups at the *meso*-positions, which decreased the π-electron density of NCP and thus increased the conformational flexibility for facile inversion of the *confused* pyrrole ring, accelerated the reaction. On the other hand, the replacement of the inner C–Br to C–NO$_2$ decreased the NFP formation probably due to the change of activity of the leaving Br group on the *confused* pyrrole.

The DFT calculation at the B3LYP/6-31G** level on *normal* and *inverted* conformation of porphyrin and N-confused porphyrin tautomers[78] by Latos-Grażyński *et al.* revealed the energies between the two conformations were 45.56 kcal mol^{-1} in porphyrin and only 18.50 and 17.55 kcal mol^{-1} in inner 3H and 2H type of NCP, respectively. Interestingly, among the *inverted* conformations of porphyrin and two tautomers of NCP, that of inner 3H NCP was the most stable compared to inner 2H NCP (+3.60 kcal mol^{-1}) and porphyrin (+6.64 kcal mol^{-1}). These theoretical study implied that the *inverted* form of NCP (**2**) was an intermediate form of the transformation from NCP to NFP and, furthermore, the tautomerism *between two tautomers of NCP*.

Very recently, the ring inversion of porphyrin heteroanalogs was reported by Latos-Grażyński *et al.*[79] Interestingly, the tellurophene ring in ditelluraporphyrin (**9**) was outwardly *inverted* with a 123° angle to the porphyrin mean plane in the solid state. The flipping of the two heterocyclic rings in solution was also suggested from the ^{1}H NMR study. The incorporation of larger heteroatoms in the pentacyclic ring would make the porphyrin core distorted and weaken the aromaticity to facilitate the ring inversion (Scheme 12).



9 (*inverted*)   **9** (*normal*)   **9** (*inverted*)

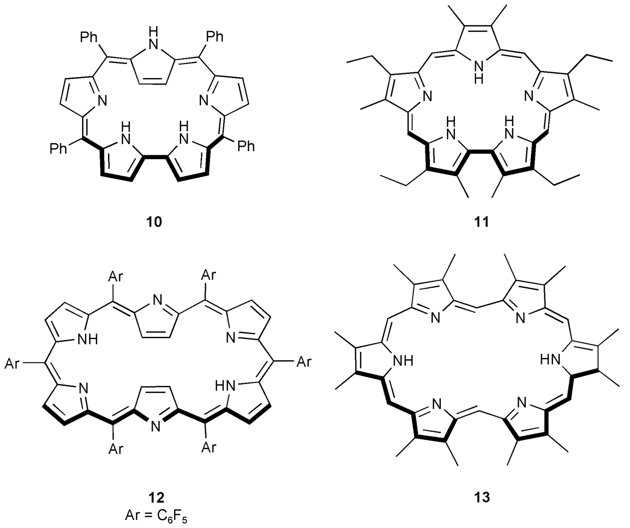
Scheme 12 Inversion of tellurophene rings in ditelluraporphyrin (**9**).

Expanded porphyrins bearing *inverted* moieties

The first expanded porphyrin of *meso*-aryl type, *meso*-tetraphenylsapphyrin (**10**), was isolated from the acid catalyzed pyrrole–arylaldehyde condensation by Latos-Grażyński and co-workers in 1995.[80,81] The uniqueness of this *meso*-tetraaryl system was documented by the dynamic *inversion* of a pyrrole ring upon protonation and deprotonation, which was not observed in the corresponding *meso*-free β-alkyl-substituted sapphyrin (**11**) (Chart 3).[82]

meso-Aryl hexaphyrin (**12**),[83,84] synthesized by Neves *et al.* in 1999, formed a distorted rectangular macrocycle by *inversion* of two pyrrole rings. Hexaphyrin **12** showed 26π aromaticity, which was inferred from the resonances of inner NH at -1.98 ppm and inner β-CH at -2.43 ppm. The corresponding *meso*-free β-dodecaalkylhexaphyrin (**13**), on the other hand, was shown to have a structure with six pyrrole nitrogens facing inwardly from the NMR spectra.[85] The pyrrolic ring in **13** was flexible and changed largely when it complexed with metal ions. For example, Zn(II) ion was coordinated by two nitrogen in a bidentate fashion in the core, whereas Pd(II) ion was shown to drive two pyrrole rings *inverted* so as to be used for coordination with their outer pointing nitrogen.[86]

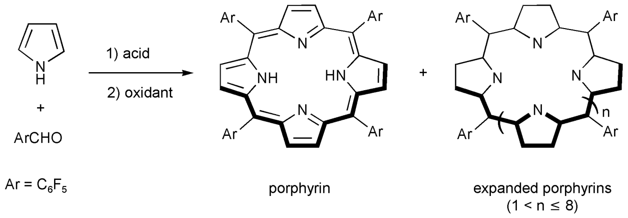
A set of higher homologs of *meso*-aryl substituted expanded porphyrins were synthesized by the one-pot condensation of pentafluorobenzaldehyde and pyrrole (Scheme 13).[24,25] The X-ray structures of *meso*-aryl octaphyrin (**14**) and trifluoroacetic (TFA) salt of nonaphyrin (**15**), showed more flexible structures with twisted ‘figure-eight’ and large ‘cleft’ conformations, respectively (Chart 4, Fig. 10). Here again, the *inverted* pyrrole conformation was adapted to release the strain of the macrocycles.



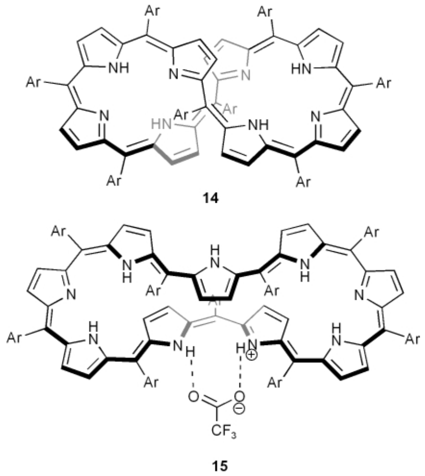
10   **11**

12
Ar = C$_6$F$_5$ **13**

Chart 3 *Meso*-substituted and *meso*-free sapphyrins and hexaphyrins.



Scheme 13 One-pot synthesis of expanded porphyrins.



14

15

Chart 4 *Meso*-aryl octaphyrin (**14**) and nonophyrin (**15**)-TFA complexes.

Sessler *et al.* synthesized [26]hexaphyrin(1.1.1.1.0.0) (**16**) of an all-aza type,[87] which possessed an *inverted* pyrrole moiety. In place of pyrrole, partial introduction of heteroaromatics such as thiophene makes a macrocyle quite different from its all-aza derivative. Chandrashekar *et al.* reported the first structural characterization of planar, aromatic 34π octaphyrin (**17**),[88] in which two of the four thiophene or selenophene rings were *inverted*. The *inverted* thiophene rings were canted only 4.67° to the mean plane defined by four *meso*-carbons. The hetero rubyrin (**18**) containing both furan and thiophene rings also

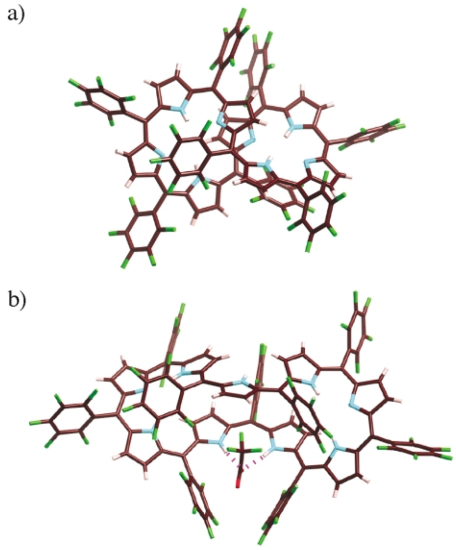
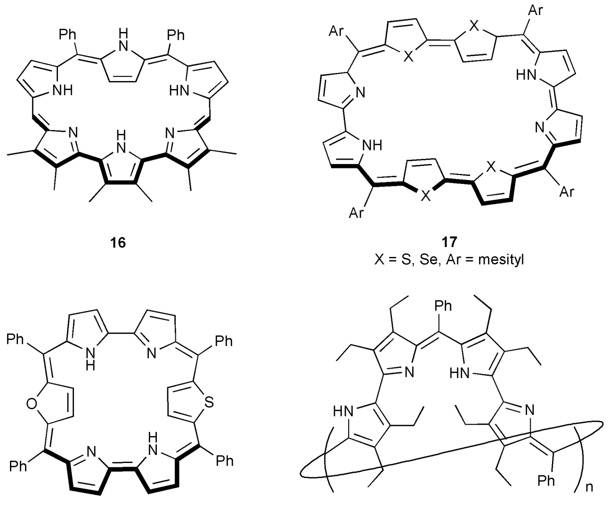


Fig. 10 X-ray structures of expanded porphyrins bearing C_6F_5 group, (a) octaphyrin (**14**), and (b) nonaphyrin (**15**)-TFA complex.

showed the *inverted* arrangement of the heterocyclic rings.[89,90]

As an example of larger pyrrolic macrocycles, Setsune *et al*. have synthesized giant cyclopolypyrrole (**19**) containing up to 24 pyrrole units from the condensation of two kinds of bipyrrole derivatives.[91,92] The structure containing 16 pyrrolic units (**19**, $n = 4$) was elucidated by X-ray crystallography, which showed a square pillar structure with a tetragonal cut end of 18.8 × 16.3 Å. Such giant porphyrinoids are potential host molecules to bind anion and/or neutral molecule in the cavity (Chart 5).



16

17
X = S, Se, Ar = mesityl

18

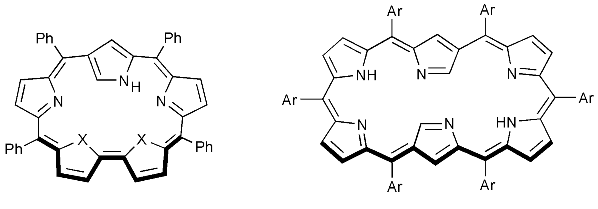
19
n = 2 - 6

Chart 5 Inverted expanded porphyrins with *meso*-aryl groups.

Expanded porphyrins bearing *confused* moieties

Recently, Chandrashekar's group and ourselves reported an N-confused sapphyrin with hetero atoms, that was synthesized from the acid catalyzed condensation of N-confused tripyrrane and bithiophene or biselenophene.[93] X-ray analysis of dithia-derivative (**20**, X = S) revealed that the *confused* pyrrole was *inverted* into the inner core and canted 25.17° to the porphyrin plane with hydrogen bonding interactions between inward NH of *confused* pyrrole and neighboring and adjacent pyrrolic nitrogens in the core.

Very recently, we have synthesized a doubly N-confused hexaphyrin (**21**) by the acid catalyzed condensation from N-confused tripyrrane and pentafluorobanzaldehyde.[94] The two *confused* pyrrole rings of **21** were *inverted*; thus, the six nitrogens and two carbons in total could provide two metal coordination sites in the core (Chart 6).



20
X = S, Se

21
Ar = C_6F_5

Chart 6 Confused expanded porphyrins.

Expanded porphyrins bearing a *fused* moiety

Among the products of a one-pot synthesis of *meso*-aryl expanded porphyrins, pentaphyrin was obtained in a *fused* form, N-fused pentaphyrin (**NFP$_5$**), which contains a *fused* tripentacyclic core like NFP (**8**) (Fig. 11).[24] At present, **NFP$_5$** is thought to be generated by the oxidation of normal pentaphyrinogen (**22**) *via meso*-arylpentaphyrin (**23**) as shown in Scheme 14. **NFP$_5$** exists as two oxidation states: a 24π anti-aromatic reduced type (**NFP$_5$-[24]**) and a 22π aromatic oxidized type (**NFP$_5$-[22]**), whose synthetic ratio changes greatly according to the amount of oxidant used. The interconversion between **NFP$_5$-[24]** and **NFP$_5$-[22]** readily occurs upon treatment with DDQ and $NaBH_4$. β-Alkyl substituted pentaphyrin previously reported by Gossauer *et al*. was 22π aromatic and had no *inverted* or *fused* structure due to the substituents at the β-pyrrolic position.[19,95] The finding of a *fused* tripentacyclic ring structure in **NFP$_5$** indicated that the *inverted* conformation of a *normal* pyrrole ring in the expanded porphyrin could also trigger the formation of a *fused* system just like an inversion of a *confused* moiety in NCP.[76,77]

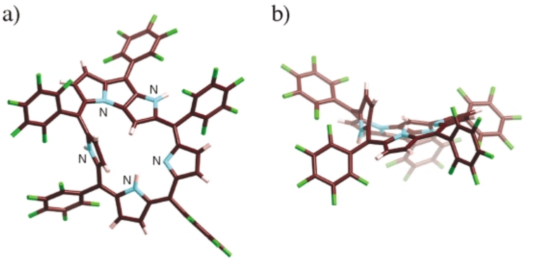
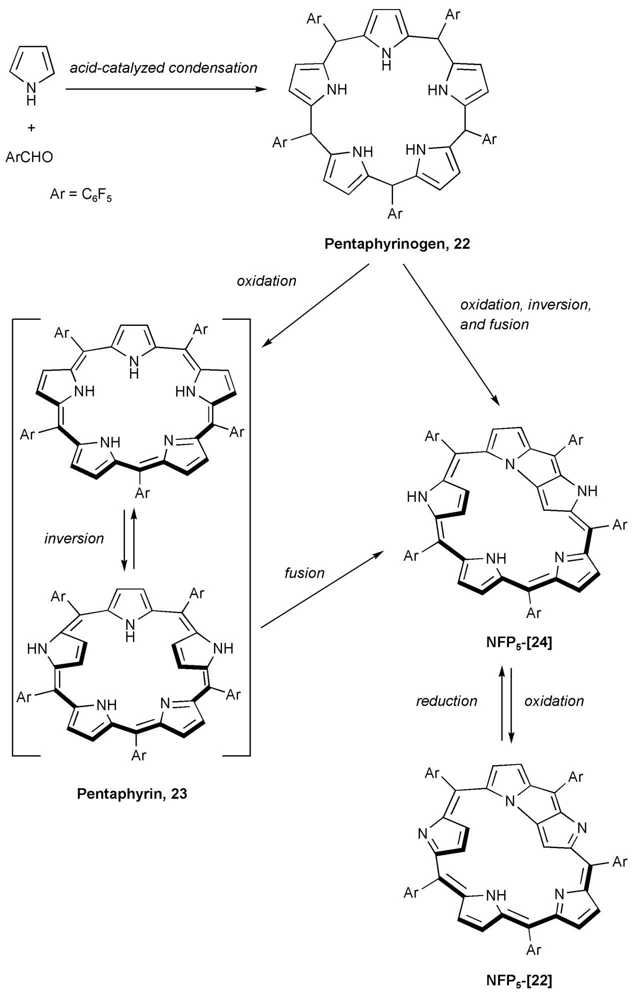


Fig. 11 X-ray structure of N-fused pentaphyrin (**NFP$_5$-[24]**) bearing C_6F_5 group, (a) top view and (b) side view.

Concluding remarks

The chemistry of porphyrin analogs containing *confused* and *inverted* moieties have been reported. Not only the unique properties of coordination modes, structures, and spectroscopic details, but also the important role of *confusion* and *inversion* for the transformation to the novel porphyrinoids has been emphasized. A basic concept derived from the study on NCP chemistry is that the incorporation of *confusion* and/or *inversion* to the oligopyrrolic macrocycles makes the compounds less stable compared to the standard framework, hence facilitating transformations to novel compounds, in other words, '***creation** from the* ***confusion***'. The decreasing of the border between the inside and outside by *inversion* recalls *Escher's artworks*. We



Scheme 14 A possible reaction pathway of NFP_5 synthesis.

believe the porphyrin analogs as shown in this article are not merely '*mutants*' in the porphyrin world but rather the majority of the porphyrinoids realm. The potential for further transformation to new porphyrinoids would make the *mutants* more attractive. The creation of new materials based on these *mutants* could be triggered by other factors, *e.g.* metal coordination. Even more characteristic features of the porphyrin analogs, which are not observed in normal porphyrins, could be disclosed expectedly or unexpectedly in the near future.

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