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The development of artificial porphyrinoids embedded with functional building blocks

Zhikuan Zhou and Zhen Shen

In this review article, we summarize the recent advances of artificial porphyrin scaffolds containing various functional building blocks as replacements for pyrrole subunit. These functional moieties are classified into three types: (i) monomeric five/six-membered heterocycles; (ii) linear oligomeric heterocycles; and (iii) aromatic ring-fused heterocycles. The main focus of this article is to compare the influence of these functional building blocks on the photophysical and aromatic properties of the incorporated porphyrinoids. These artificial porphyrinoids are excellent candidates not only for the basic study on the aromaticity of macrocycles, but also for many potential applications such as near-infrared (NIR) dyes, magnetic materials, molecular switches and nonlinear optical materials.

1. Introduction

Natural porphyrins, such as chlorophyll and heme, play important roles in electron transportation and biochemical processes. Porphyrin can be seen as a planar conjugated macrocycle constructed with four pyrrole units that are connected via their \( \alpha \) position by methine carbons. Typically, there are 18 delocalized \( \pi \) electrons in the conjugation pathway in a porphyrin scaffold. Due to the macrocyclic and aromatic features, porphyrins exhibit distinguished photophysical and chemical properties, such as strong absorption in the UV-visible region, redox interconversion and metal coordination.

To meet the requirements for applications in material science, various synthetic strategies have been employed to construct novel artificial porphyrin homologues, such as meso- and \( \beta \)-substitution, ring-contraction and ring-expansion, isomerization and core-modification, with the main purpose of regulating their structural and electronic properties. Fig. 1 shows the representative skeletons of porphyrinoids. From the structural point of view, expanded porphyrins, such as sapphyrin, pentapyrin and hexapyrin, can be viewed as the replacement of a pyrrole subunit by a bispyrrole, a dipyrromethene or tripyrrane, respectively. In the case of rubyrin, it can be regarded as the replacement of two pyrrole subunits by two bispyrrole moieties. The conjugation and aromaticity are maintained in the porphyrin-like scaffolds, meanwhile, they possess novel photophysical and electronic properties due to their unique structures. For example, the flexible \( \pi \)-conjugated conformation and large aromatic features of expanded porphyrins exhibit strong absorption and fluorescence in the near-infrared (NIR) region, anion binding property and considerable two-photon-absorption cross-section values, which make them good candidates as NIR dyes, anion probes and non-linear optic materials.

Fig. 1 Representative porphyrin scaffolds. (Pentagons represent five-membered rings such as pyrrole and chalcogen-substituted heterocycles)

In this review article, we regard porphyrin as a scaffold in which one or more pyrrole subunits can be replaced by other five or six-membered rings or small conjugated moieties, which are commonly used in polymer material science. The intriguing structural and electronic properties of these porphyrin-like...
networks influenced by the conformation and electronic feature of these functional subunits were summarized. Furthermore, their applications in material science were also reviewed.

2. Porphyrinoids embedded with functional building blocks.

2.1 Synthetic methodologies

Several synthetic methodologies have been developed since the first artificial porphyrinoid was reported in the early of 20th century. The general synthetic methods include one-pot and stepwise procedures, which were summarized in Scheme 1. Under Lindsey condition,\(^\text{14}\) acid catalyzed condensation of pyrrole, aldehyde and diol followed by oxidation with oxidants such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or p-chloranil, afforded mono-substituted core-modified porphyrins. While Ulman condition\(^\text{15}\) provided a facile synthesis of bis-substituted symmetric core-modified porphyrin. “3+1” method developed by Broadhurst\(^\text{16}\) and its modified condition\(^\text{17}\) were commonly used for stepwise synthesis of asymmetric porphyrins. Other efficient methods for incorporation of subunits are MacDonald “2+2” type reaction\(^\text{18}\) and its modified method.\(^\text{19}\) The “1, 2, 3” in the cyclization method refers to the number of heterocycles within the precursors used for acid catalyzed condensation.

From the synthetic point of view, various artificial functional porphyrinoids can be assembled by introducing the functional subunits into diol (1 and 7), dialdehyde (2 and 5) or tripyrrane (4) precursors using the methods described in Scheme 1.

2.2 Building blocks

Most of the π-conjugated building blocks that are used to permute pyrrole units in a porphyrin skeleton are summarized in Fig. 2. We classified these building subunits into three types based on their structural and electronic features. Type I consists of simple five- or six-membered heterocycles. Type II are heterocyclic oligomers linked either directly or through bridged atoms such as vinyl group. Type III contains heterocycles in ring fused fashion.

Each type of building blocks possesses unique structural and electronic features, which will influence the conformation, photophysical and chemical properties of the incorporated tetra-unit or expanded porphyrin scaffolds.

2.3 Porphyrinoids embedded with type I building blocks.

This type of building blocks consist small five-membered cyclic molecules, such as N-confused pyrrole,\(^\text{20}\) chalcogen-containing heterocycles \(^9\),\(^\text{21}\) indene \(^16\) and azulene \(^17\),\(^\text{22}\) or six-membered heterocycles such as benzene and pyridine (Fig. 2). They can be feasibly incorporated into porphyrin and oligopyrrole-like systems and have been extensively studied and reviewed elsewhere.\(^\text{23}\) In this section, we mainly focus on the porphyrin skeletons containing some intriguing building blocks in type I.

Scheme 2 Synthesis of carthathiaporphyrin 35. TEA = Triethylamine.
Fig. 3 Absorption spectra of 34 (solid line), 35 (dotted line), 34-Pd (short dashed line), and 35-Pd (long dashed line) in CH₂Cl₂. Reproduced from Ref. 22 with permission from Wiley.

Recently, Latos-Grażyński et al. reported acabathia-porphyrin 35 containing cyclopentadiene subunit (Scheme 2).²⁴ 35 was prepared by [3+1] condensation of a mixture of isomeric tripyrrane 33 and thiophenediols. After first oxidation with p-chloranil, a stable aromatic chlorine-like derivative 34 was obtained, further carefully oxidation with one equivalent of DDQ yielded the target 18α-cabathiaporphyrin 35. 34 exhibits a relatively broad Soret band at 417 nm, while 35 displays split Soret bands at 415 and 441 nm (Fig. 3, left). Both compounds are aromatic with a set of weak Q bands (Fig. 3, right). Their Pd-complexes 34-Pd and 35-Pd were investigated for the first time which showed distinct change in the absorption spectra. The N₂SC core based on the existence of cyclopentadiene make porphyrins 34 and 35 excellent macrocyclic ligands to coordinate with various metal ions like other cabaporphyrins.²⁵

Scheme 3 Synthesis of expanded porphyrin 37 and its dicopper complex 38.

Fig. 4 UV-Vis-NIR absorption spectra of 38 recorded during electrochemical oxidation in CH₂Cl₂, 38 (black line), [38]⁺ (dark gray line), and [38]²⁺ (light gray line) are highlighted. Isosbestic points are indicated via black circles. Adapted with permission from Ref. 27. Copyright 2013 American Chemical Society.

Inspired by the excellent ability to provide polydentate binding sites as bridging ligands in multinuclear transition metal complexes, Meyer et al. employed pyrazole²⁶ as a building block to construct hexaphyrin-like²⁷ expanded porphyrin framework 37 (also called Siamese-twin porphyrin).²⁸ 37 was synthesized in satisfactory yield through Lindsey type cyclization of pyrazole-containing tripyrrane 36 and benzaldehyde. The ingenious design resulted in two adjacent tetraporphyrin-like coordination cavities in one skeleton, although the entire macrocycle showed non-aromatic properties due to the broken π-conjugation pathway at the pyrazole units. Stable dicopper(II) complex 38²⁹ was prepared, which can be easily converted to [38]⁺³⁰ by oxidation with AgBF₄ or electrochemical procedure (Fig. 4). As revealed by X-ray analysis, two-fold oxidized [38]²⁺ adopted similar twisted helix fashion structure with 38, in which two copper were tetragonal coordination. [38]²⁺ is a ligand-centered radical species with invariant copper oxidation state (Scheme 3). Electronic interaction between two copper in close proximity combined with the impact of potentially noninnocent expanded porphyrin ligand made 38 a valuable platform with rich redox chemistry, which may find application in bioinspired multi-electron processes.

Shen et al. have employed phenanthrene ring fused pyrrole 19 to increase the rigidity and π-conjugation in BODIPY and porphyrin molecules.³⁰, ³¹ They successfully synthesized core-modified porphyrin 39 by the condensation reaction of pyrrole 19 and thiophenediols using Ulman method ¹⁵ in 18 % yield.¹² The incorporation of phenanthrene fused pyrrole efficiently extended the π-conjugation of porphyrin and redshifted its Soret and Q bands to 514 and 837 nm in CHCl₃, respectively. Moreover, the emission band of 39 centered at λ > 900 nm. The build-in phenanthrene fused pyrrole moieties caused considerable steric hindrance with the meso-phenyl substituents, thus force the π-system to adopt a heavily distorted saddle-like structure. Zeng and Shen et al. further investigated the 2D self-assembly behavior of 39 on a highly-oriented pyrolytic graphite (HOPG) surface by high-resolution STM.³³ Interestingly, when 39 was added into a non-polar solvent, such as n-tetradecane and l-phenyloctane, the macrocycle framework assembled into a saddle-form architecture, while in polar solvent, such as
heptanoicacid, the conformation is totally reversed (Fig. 5). The results showed that core-modified porphyrin embedded with phenantherene fused pyrrole may form highly ordered 2D network in solid-liquid interface, which made it possible to fabricate porphyrin-based devices.

Scheme 5 Synthesis of core-modified porphyrin 42 embedded with isothianaphthene 15.

Isothianaphthene (ITN, or benzo[c]thiophene, 15) is a widely used precursor for small bandgap linear π-conjugated polymers34 due to its contribution to π-extension. The poor stability and complicated synthetic procedure have impeded its application until Ono et al.35, 36 reported a facile and efficient retro-Diels-Alder strategy, in which soluble bicyclo[2.2.2]octadiene (BCOD) thiophene 40 precursor was employed to convert into ITN quantitatively by heating under vacuum. As shown in Scheme 5, Shen et al reported the reaction of lithium salt of 40 with p-fluorobenzaldehyde to give its diol compound which condenses with phenantherene fused pyrrole 19 to form soluble porphyrin 41.32 Core-modified porphyrin 42 embedded with both ITN and phenantherene-fused pyrrole subunit was successfully synthesized from 41 by heating at 300°C under vacuum quantitatively. The aryl-fused thiophene and pyrrole units in 42 extended the π-conjugation of normal porphyrin thus showed redshifted Soret band at 543 nm and Q bands at 712 and 866 nm, made it possible for application as near IR dyes.

Scheme 6 Synthesis of phosphaporphyrins 47-49 and 52.

In addition to carbon and chalcogen atoms, other elements such as phosphorus and silicon have been employed to replace the core nitrogen atoms of porphyrins to perturb their electronic structures. Imahoriet al. successfully introduced phosphate unit into porphyrin to obtain phosphaporphyrins 45 and 46.37, 38 The key synthon P-masked phosphatripyrane 43 was synthesized through a carefully designed route, which was condensed with thiophene or pyrrolediol compound 1 under BF3·Et2O catalyzed [3+1] condition to afford porphyrinogen 44. After desulfurization with P(NMe2)3 and oxidation with DDQ, 45 and 46 were obtained as stable solids which slowly decomposed in solution when exposed to air and light. The durability of the +3 valence state P center to acid and oxidant were dramatically improved through introduction of electron-withdrawing pentafluorophenyl group onto the phosphorus atom. It was revealed that expended phosphaporphyrins 52 was chemically stable and structurally rigid with only slightly perturbed aromaticity and electronic properties (Scheme 6).39

![Fig. 6 UV-vis absorption spectra of 47 (a, red) and 48 (b, green). The spectra of 45 and 46 were shown in black lines in a and b, respectively. Reproduced with permission from Ref. 36. Copyright 2010 American Chemical Society.](image)

![Fig. 7 Bond lengths of 49 determined by X-ray (black) and DFT calculation (blue), NICS values (red). Adapted with permission from Ref. 39. Copyright 2008 American Chemical Society.](image)

Relatively smaller HOMO-LUMO band gaps were found for phosphaporphyrins 45 and 46 compared with regular porphyrins. Thus, they showed redshifted Soret and Q-bands (45: 431 and 698 nm; 46: 440 and 718 nm). The phosphorus center in phosphole unit can be easily functionalized by oxidation, substitution or complexation with metal ions such as Ni2+, Pd2+ and Pt2+.46 Unique aromaticity switching properties were found for both 18-π aromatic 45 and 46 by oxidation with H2O2 (Scheme 6). The fused cyclopentane subunit and phosphorus center of phosphole were oxidized to cyclopentadiene and phosphoryl, respectively, which resulted in the extension of π-conjugation pathway of 45 and the formation of a 22-π aromatic system 47. While in the case of 46, oxidation only occurred at phosphorus center, thus afforded a 20-π antiaromatic system 48.38 The aromatic 47 showed split Soret bands at 422 and 494 nm with broad Q band at 964 nm, while antiaromatic 48 exhibited high-energy region absorption band at 394 nm and no obvious Q band (Fig. 6). Furthermore, due to the high affinity between P and metal atoms, complexation of
with zero valence group 10 metals afford stable 20-π antiaromatic isophlorin complexes. Alternative single-double bond derived from X-ray data combined with DFT calculation and nucleus-independent chemical shifts (NICS) value\(^{41, 42}\) (close to zero, Fig. 7), clearly demonstrated the antiaromatic properties of Pd complex\(^{49}\).\(^{43}\)

Through a one-pot reaction of silolediol 53, pyrrole and p-tolylaldehyde catalyzed by BF\(_2\)-EtO and oxidation by DDQ subsequently, only small amount of phlorin-like compounds that were aromatic. Methane sulfonic acid (MSA) catalyzed condensation of silatryptophorphan 58 and pentafluorobenzaldehyde followed by oxidation with DDQ generated a stable hexaphyrinoid 59 instead of the desired macrocycle 60.\(^{45}\) Although conjugated porphyrin-like macrocycles embedded with silole were not trapped, the above results presented detailed studies on the reactivity of silole within porphyrin environment.

![Scheme 7 Synthesis of porphyrinoids containing silole units.](image)

Scheme 7 showed two examples of attempt to synthesize porphyrinoids 56 and 60 that embedded with silole 13 moieties. Through a one-pot reaction of silolediol 53, pyrrole and p-tolylaldehyde catalyzed by BF\(_2\)-EtO and oxidation by DDQ subsequently, only small amount of phlorin-like compounds 54 and 55 were obtained.\(^{44}\) Further oxidation with DDQ resulted in the formation of an unexpected iso-carbacorrole 57 rather than the desired porphyrin-like product 56. Coordination with Cu and Ag converted non-aromatic iso-carbacorrole 57 into its complexes that were aromatic. Methane sulfonic acid (MSA) catalyzed condensation of silatryptophorphan 58 and pentafluorobenzaldehyde followed by oxidation with DDQ generated a stable hexaphyrinoid 59 instead of the desired macrocycle 60.\(^{45}\) Although conjugated porphyrin-like macrocycles embedded with silole were not trapped, the above results presented detailed studies on the reactivity of silole within porphyrin environment.

![Scheme 8 Synthesis of benziporphyrins 63 and 64.](image)

Scheme 8 Synthesis of benziporphyrins 63 and 64.

Six-membered rings such as benzene and pyridine are typical 6-electron aromatic molecules. When introduced into a porphyrin framework, their local aromaticity usually impedes the global π-conjugation of the macrocycles. For example, in benziporphyrin 63,\(^{46, 47}\) benzene unit was linked with the tripyrrolic brace through 1, 3-position, this resulted in the loss of π-electron delocalization in the whole molecule which turned out to be non-aromatic. By changing the connection fashion of benzene into 1,5-position (Scheme 8), an aromatic benziporphyrin 64 was achieved.\(^{48}\) The chemical shifts of inner CH protons a and b appeared at upper-field 2.32 ppm, while the out ones c and d at 7.68 ppm (168K), clearly demonstrated the existence of a diatropic ring current. These results were consistent with the observed reduction of bond lengths of phenylene subunit (1.365-1.390 Å). Similar phenomenon that different build-in manners of subunits lead to distinct diversity of properties was also found in porphyrin embedded with naphthalene 18,\(^{49, 50}\)

![Scheme 9 Synthesis of expanded porphyrin and its uranyl complex.](image)

Scheme 9 Synthesis of expanded porphyrin 67 and its uranyl complex 68.

![Fig. 8 Left: UV-Vis spectra of 67 and 68 in CH\(_2\)Cl\(_2\); right: ACID plot of 68. Adapted with permission from Ref. 47. Copyright 2014 American Chemical Society.](image)

Fig. 8 Left: UV-Vis spectra of 67 and 68 in CH\(_2\)Cl\(_2\); right: ACID plot of 68. Adapted with permission from Ref. 47. Copyright 2014 American Chemical Society.

Recently, Sessler et al reported the construction of a pyridine-containing expanded porphyrin 67 through Pd(II)-catalyzed Suzuki coupling of 2,6-dipyrrolylpyridine diborate 65 and dibromo compound 66 in 30% yield (Scheme 9).\(^{51}\) The absorption of this macrocycle showed high-energy Soret-like band at 351 nm without obvious Q band, which indicated its non-aromatic feature. Interestingly, upon complexation with large uranyl cation, the dianionic form of 67 was stabilized and an aromatic complex 68 was achieved. Two sharp Soret-like bands at 389 and 486 nm accompanied by three Q-like bands at 681, 847 and 1177 nm demonstrated its aromatic feature. Anisotropy of the induced current density (ACID)\(^{52, 53}\) plot of 68 exhibited a diatropic ring current (Fig. 8, clockwise, red arrows) around the macrocycle, clearly supported the fact that complexation with anion increased the aromaticity of macrocycle.

### 2.4 Porphyrinoids embedded with type II building blocks.

The type II building blocks in Fig. 2 are composed of two or more five-membered heterocycles that are linked at α or β position directly (20-22) or by unsaturated bridges (23, 24). Permutation of pyrrole units in normal porphyrin by these larger-size subunits usually leads to the expansion of porphyrin framework into sapphyrin-, rubyrin- or hexaphyrin-like...
macrocycles. These functional subunits incorporated expanded porphyrins have more attractive properties than normal tetrapyrrole porphyrins such as absorption and fluorescence in the near-infrared (NIR) region, better anion binding ability, flexible structure and aromatic switching.

![Scheme 10 Synthesis of core-modified rubyrins 69 and 70.](image)

**Scheme 10 Synthesis of core-modified rubyrins 69 and 70.**

Fig. 9 Absorption and emission spectra of 69 in CHCl₃ (λₑₓ = 532 nm). Inset shows two conjugation pathways in 69. Reproduced from Ref. 49 with permission from Wiley.

Bithiophene is a commonly used building block to extend conjugated framework of porphyrin into rubyrin which showed red-shifted absorption and better anion binding property. Shen et al. reported a core-modified rubyrin 69 with build-in bithiophene 20 and phenanthrene-annulated pyrrole 19 (Scheme 10). Ring fusion led to a cross-conjugated 26- and 52-π hexaphyrin 69, which displayed a Soret band at 596 nm and three Q bands at 714, 784 and 1076 nm (Fig. 9). The steric hindrance between phenanthrene-annulated pyrrole and peripheral fluorophenyl groups forced rubyrin 69 to adopt a bowl-shaped structure, which effectively prevents self-aggregation. Simple test strips that were made by embedding 69 into a polyurethane membrane were used for rapid Hg²⁺ screening in aqueous solution.

![Fig. 10 Structure and function of pH-activatable 70 for ¹O₂ generation.](image)

**Fig. 10 Structure and function of pH-activatable 70 for ¹O₂ generation.** Adapted with permission from Ref. 50. Copyright 2013 American Chemical Society.

By using the same strategy, biselenophene unit was introduced into a porphyrin skeleton to form rubyrin 70 with near-infrared absorption and emission. Due to the heavy atom effect, the selenium atom enhanced the ¹O₂ generation efficiency, meanwhile, the peripheral dimethylaminophenyl groups led to the pH-controllable activation of 70 (Fig. 10). High singlet oxygen quantum yield (Φ₅) was obtained under NIR irradiation (635 nm) at acidic condition (Φ₅=0.69, pH=5.0), while 70 was deactivated at physiological pH (Φ₅=0.06, pH=7.4). The 70-loaded nanoparticle functionalized with cancer cell-targeting reagent folate was designed and used as an acidic pH-activatable targeted photosensitizer for selective NIR photodynamic therapy against cancer.

**Scheme 11 Synthesis of core-modified rubyrin 72.**

Expanded porphyrin 72 which contains two terthiophene units 22 has been synthesized via an p-methylbenzene sulfonic acid catalyzed [5+5] MacDonald condensation of modified pentapyrane 71 and pentafluorobenzaldehyde (Scheme 11). The increase in the number of thiophene unit extended the π-conjugation. Macrocycle 72 possessed planar conformation and exhibited high two-photo absorption cross-section value of 108000 GM with respect to Rhodamine-6G reference, which made it possible for applications in the field of nonlinear optical devices.

**Scheme 12 Synthesis of vinylogous expanded isophlorins 73 and 74.**

![Fig. 11 Changes in the UV/Vis absorption spectra of 74 (gray solid line) upon addition of TFA (black solid line) followed by triethylamine (dotted line). CA = [CF₃COO]⁻.](image)

**Fig. 11 Changes in the UV/Vis absorption spectra of 74 (gray solid line) upon addition of TFA (black solid line) followed by triethylamine (dotted line). CA = [CF₃COO]⁻.** Adapted from Ref. 53 with permission from Wiley.

In planar or near-planar conjugated systems, aromaticity and antiaromaticity were determined via Hückel’s (4n+2) and 4n π-electron rule. Altering the number of building blocks or the
connection pattern between them is a widely used method to tune the number of π-electrons in conjugated macrocycles. Ethylene bridged bis(thiophene)/furan 23 were employed to synthesize two stable antiaromatic 32π expanded isophlorin 73 and 74 (Scheme 12). The crystal structure analysis of 73 revealed that there were unprecedented intermolecular F···S, C–H···F and π–π interactions which are very rare for antiaromatic system. With four furan rings, 74 adopted ring-inverted conformation. In the neutral form, 74 exhibited split Soret band at 430 and 482 nm without obvious Q-like bands, while upon addition of TFA or oxidant such as [EtO'SbCl5], the Soret band redshifted to 580 and 611 nm accompanied by appearance of two Q bands between 800 to 1000 nm. Triethylamine or reductant such as FeCl3 could reduce the dication form of 74 to its neutral form (Fig. 11). 1H NMR confirmed the reversibility between 4n π and (4n+2) π states of 74 by suitable redox conditions.

Scheme 13 Synthesis of dithienylethene containing core-modified rubyrins 78 and 79.

Fig. 12 ACID plots of 78 (a) and 79 (b) at an isosurface value of 0.065. Reproduced from Ref. 56 with permission from Wiley.

Another possible way to tune the aromaticity of porphyrinoid is to incorporate stimuli-responsive building blocks into porphyrin skeleton. Dithienylethene 24 is an excellent candidate which exhibit switchable open-closed conformation interconversion in response to light or certain redox potential. 60, 61 Core-modified rubyrins which contain one and two dithienylethene moieties 78 and 79 were synthesized starting from the corresponding diol compound of 24 via [4+1] and Ulman condition, respectively (Scheme 13). Probably due to the ring strain, the dithienylethene unit in aromatic 78 adopted a closed-form conformation, while in non-aromatic 79, one of the two dithienylethene units adopted an open-form conformation which was confirmed by X-ray analysis, NMR and UV-Vis spectrum. ACID plot of 78 showed a clear clockwise ring current which indicated the 26π aromatic feature of the conjugated system. In contrast, no obvious ring current was found along the outer ring periphery of 79 (Fig. 12). The structure of dithienylethene does have an impact on the aromaticity of macrocycles, it is possible to construct proper conjugated porphyrinoids with build-in dithienylethene moieties to form stimuli-active molecules for applications in molecule switch.

2.5 Porphyrinoids embedded with type III building blocks.

The type III building blocks in Fig. 2 are composed of two or more five or six-membered heterocycles that are connected in fused fashion. From the structural and synthetic point of view, it is possible to embed these building blocks into tetra-unit or expanded porphyrin skeleton. All these building blocks are π-conjugated molecules with rigid conformation which have the ability to extend the π-conjugation of porphyrinoids and increase their structural rigidity. Some of them possess unique electronic structure that may perturb the conjugation pathway of porphyrinoids when incorporated into their framework (such as 25-26). 29-32 contain fused benzene or pyridine unit, it is fascinating to investigate the global electronic property of porphyrinoids that embed with these subunits having local π-conjugations.

Scheme 14 Synthesis of core-modified porphyrins 81 and 82 embedded with ferrocene and ruthenocene.

As a pioneering work, Latos-Grażyński et al employed core-modified porphyrin as a platform to investigate the electronic conjugation across metalloocene in a fully conjugated macrocycle. Ferroenothiaporphyrin 81 and ruthenocenoporphyrin 82, which possess a build-in ferrocene and ruthenocene unit, respectively, were synthesized via [3+1] cyclization reaction (Scheme 14). Distorted conformation of both 81 and 82 were demonstrated by X-ray structure analysis. 1H NMR data revealed the antiaromatic nature of molecules 81 and 82, while their two-electron reduced congeners 83 and 84 showed clear aromatic properties. It provided a possibility that the macrocyclic π conjugation can transmit across a d-electron metalloocene to form a three-dimensional aromatic system.

Scheme 15 Synthesis of heteroporphyrin 88 containing thienopyrrole unit.
Shen et al. reported a heteroporphyrin 88° embedded with a thienopyrrole unit through TFA-catalyzed condensation of dialdehyde 85 with reactive diacid 87° which was prepared in situ from debenzylation of 86 by catalytic hydrogenation (Scheme 15). 88° exhibited a near-planar conformation in the solid state. The relatively broad absorption bands at 356 nm and 455 nm changed into an intense peak at 410 nm accompanied by several weaker bands between 500-800 nm upon reduction by NaBH4 or a controlled electrochemical reduction at potential Eapp = -1.35V. Due to N-H tautomerism, the thienopyrrole unit acted as a switch to tune the aromaticity of heteroporphyrin between the stable nonaromatic 88° and 20π antiaromatic 89° under proper redox condition. The ACID isosurface plot for 88° predicted relatively poor electron conjugation, as there is a disrupted pattern within the electronic current. Its tautomer 89° contains counterclockwise currents, which means a stronger antiaromatic ring current is generated in the tautomer that has a 20 π-electron conjugation system. (Fig. 13)

Scheme 16 Structures of heteroporphyrins 90-92 containing thienothiophene unit.

Three heteroporphyrins that contain thienothiophene as building blocks were reported. 90-92° are 22π aromatic macrocycles (Scheme 16). Annulated pyrroles in 91 and 92 contributed to the delocalization of π electrons and thus redshifted their Soret band for 56 nm compared to 90. Compound 90 showed a Soret band at 503 nm with a shoulder at 530 nm, followed by an intense Q-band at 725 nm and other two broad Q-bands at 868 nm and 957 nm. 91 showed an intense Soret band at 559 nm with three relatively weak Q-bands at 656 nm, 719 nm and 973 nm. 92 exhibited almost the same absorption peak pattern as 91. The absorption of these thienothiophene-containing heteroporphyrins well extend into the NIR region.
Scheme 18 Synthesis of porphyrin-related macrocycles 106 and 107 embedded with 1,10-phenanthroline moiety.

Scheme 19 Synthesis of sapphyrins 110 and 111 embedded with benzodipyrrrole or benzodifuran moiety.

Benzodipyrrrole and benzodifuran 30 were embedded into sapphyrin skeleton through [3+1] condensation from their diformylated derivatives 109 and tripyrromethane dicarboxylic acid 87, respectively (Scheme 19). 1H NMR analysis revealed that the inner NH protons of 1107 resided unsymmetrically as shown in Scheme 19. Free-base 110 showed a broad Soret-like band at 466 nm and a Q band at 727 nm, which appeared as an intense peak at 469 nm with a major Q band at 703 nm upon diprotonation with p-toluene sulfonic acid. It appeared that incorporation of the benzodipyrrrole unit increased the rigidity of sapphyrin network and had a strong influence on the electronic properties of the molecule. Sessler et al. incorporated benzodifuran subunit into a sapphyrin system 11178 and examined its anion binding properties. Diprotonated form of dioxabenzosapphyrin 111 was found to bind fluoride and chloride anions only weakly in MeOH. Meanwhile, molecular recognition behavior that interacted with neutral Ar-OH species was also observed.

Scheme 20 Synthesis of expanded porphyrins 112-115 embedded with naphthobipyrrole moiety.

1,10-dihydrobenzo[e]-pyrrolo[3,2-g]indole 31 (also termed as naphthobipyrrole) was a rigid and conjugated building block that is composed of a naphthalene and two fused pyrrole units. Due to the existence of two unsubstituted pyrrole α-position, naphthobipyrrole can be introduced into expanded porphyrin system by using the same synthetic method as for pyrrole.
Scheme 20 shows the preparation and structures of a series of porphyrinoids with one to four build-in naphthobipyrole moieties. The incorporation of naphthopyrrolo units imposed an conformational restriction on the porphyrin skeleton. One of the pyrrole rings adopted an inverted conformation in the freebase form of saphyrin-like macrocycle 112. Upon mono-protonation by TFA, the inverted pyrrole transformed into normal “NH in” conformation, whereas diprotonation caused re-inversion of the pyrrolic subunit. Rubyrin-like 113 exhibited spectroscopic properties consistent with aromatic 26π system. Its mono-HCl salt possessed a nearly planar conformation in the solid state. 30π aromatic cyclo[4]naphthobipyrrole 115 was obtained as a dihydrogen sulfate salt via an FeCl₃ oxidized cyclization of the alkyl-substituted naphthobipyrole. The crystal structure analysis revealed that 115 adopted a saddle-type conformation. The Q band of 115 extended well into NIR region (1276 nm) with high extinction coefficient (2.19×10⁵ M⁻¹ cm⁻¹). Interestingly, 115 showed large two-photon absorption cross section values (3.3-5.2×10⁴ GM) in 600-800 nm range, which made it a promising pigment for application in nonlinear optic devices.

Macrocycle 114 is a nearly planar 24π-electron antiaromatic molecule. It contains three rigid naphthopyrrolo subunits that are linked through methylene bridges. Upon protonation with hydrogen halides (HX), the neutral 114 was reduced to a formal 25π-electron radical dication species 118 via a proton-coupled electron transfer process. In the case of HI, further reduction produced a 26π-electron aromatic cation 116 that can also be obtained independently using the more classic reductant. Upon deprotonation, the aromatic cation 118 spontaneously reverted to the neutral 24π-electron species 114 (Fig. 16 a). This was reflected in the UV-Vis-NIR absorption spectra, in which 114 showed a broad Soret band at 462 nm, whereas 118 showed a redshifted Soret-like band at 562 nm with two weak Q-like bands at 784 and 1081 nm. While aromatic 116 exhibits a sharp Soret band at 612 nm accompanied with three Q bands at 720, 802 and 888 nm (Fig. 16 b). Due to the ability to interconvert between three well-defined oxidation states, 114 may find application in the creation of switchable electronic materials.

Carbazole-based materials have been extensively studied due to their high emission, electron conducting and chemically stable properties. Müllen et al successfully introduced two carbazole subunits into a porphyrin skeleton via a one-pot Suzuki coupling reaction of 119 and 120 (Scheme 21). The UV absorption of 121 showed two local maxima at 307 nm and 400 nm, which is typical for nonaromatic porphyrin system. Macrocycle 121 also exhibited blue emission at 427 nm with high quantum yield (Φ= 0.68, λₑₓ = 349 nm). Interestingly, upon stepwise oxidation with MnO₂, three new Q-like bands arose at 846 nm, 945 nm and 1076 nm. The supposed structure of oxidized product was 122, which is an 18π aromatic macrocycle. However, it was difficult to isolate 122 due to its poor stability. The palladium-catalyzed cross coupling method proved to be a new and efficient synthetic protocol to construct novel carbazole-containing porphyrinoids.
A multi-step cyclization strategy to incorporate carbazole into a core-modified porphyrin was reported by Maeda and Osuka et al. Macrocycle 124 was obtained by a Glaser coupling reaction from 1,8-diethynyln-carbazole 123. The thiophene and selenophene moieties in porphyrins 125 and 127 were generated in situ via the reaction of 124 with Na₂S and Se under proper conditions, respectively (Scheme 22). Both 125 and 127 are non-aromatic molecules with absorption under 500 nm. Upon oxidation with MnO₂, stable aromatic macrocycles 126 and 128 were obtained, each of which exhibited three Q-like absorption bands at 845, 934, 1049 nm and 845, 952, 1089 nm, respectively (Fig. 17). This multiple annulation protocol efficiently expanded the porphyrin synthetic methods compared to the general acid-catalyzed condensation-based synthesis. The carbazole-based porphyrins, which possess distinct aromaticity and expanded π conjugation, displayed remarkable intensified absorption that is well in the near infrared region.

3. Conclusion and outlook

In this review, we have summarized the remarkable progress in the field of synthesis and application of artificial porphyrinoids embedded with various functional building blocks. Various π-conjugated moieties with unique structural and electronic features have been incorporated into the porphyrin-like macrocycles through chemical modification. The macrocyclic porphyrin network offered a platform to embed functional building blocks which act as switches in the macrocycles to regulate the spacial conformation and aromaticity of porphyrinoids. Small five or six-membered rings such as cyclopentadiene and pyridine can be embedded into both tetra-unit and expanded porphyrin skeletons. Compared with pyrrole, these building blocks affect the π-conjugation pathway and coordination properties of porphyrins with tiny conformational perturbation. Linear oligomeric subunits can efficiently extend the conjugation of porphyrin, thus redshift their absorption into NIR region. Due to the rigid conformational features, porphyrinoids embedded with fused five/six-membered heterocycles adopt planar or near planar conformation with strong absorption in the NIR region. Furthermore, the unique local aromatic features of these building blocks affect the global aromatic properties of porphyrinoids. It has been demonstrated that through rational design porphyrinoids embedded with functional building blocks exhibit many promising properties such as redox interconversion, unique metal coordination ability, aromatic switching, strong NIR absorption and emission. As promising photoelectric functional molecules, their application for photodynamic therapy, photovoltaics, molecular switch and non-linear optics need to be investigated deeply in the future. This review introduced an efficient strategy for tuning the structural and electronic properties of porphyrinoids, further researches on the incorporation of stimuli-responsive (redox, pH, light) building blocks into macrocyclic network to form switchable porphyrinoids are highly desirable.

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Notes and references

State Key Laboratory of Coordination Chemistry
School of Chemistry and Chemical Engineering
Nanjing University, Nanjing, 210093 (P. R. China)
E-mail: zshen@nju.edu.cn

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The synthesis and applications of artificial porphyrinoids containing various functional building blocks by replacements of pyrrole subunit have been summarized.