Recent developments in heteroporphyrins and their analogues  

I. Gupta, M. Ravikanth  
Department of Chemistry, Indian Institute of Technology, Powai, Mumbai 400076, India  

Abstract  
Monoheteroatom substituted porphyrins and diheteroatom substituted porphyrins resulting from the replacement of one and two nitrogen atoms, respectively, are very stable aromatic molecules possessing very interesting properties. Significant progress has been made in last 5–6 years by developing newer methods and also by modifying the existing synthetic methodologies. These have been used to synthesize several heteroanalogues of porphyrins and their derivatives including the synthesis of chlorins, corroles, confused porphyrins, covalent and non-covalent porphyrin assemblies. This article reviews the developments that have been occurred in heteroporphyrin chemistry during 1999–2005.  

Keywords: Heteroporphyrins, Confused porphyrins, Corroles, Chlorins, Covalent and non-covalent porphyrin arrays.
1. Introduction

Porphyrins are a class of conjugated macrocyclic compounds in which four pyrrole rings are linked to each other in cyclic fashion through meso-carbon bridges. These represent one of the most widely studied of all known macrocyclic systems [1]. Replacement of pyrrole nitrogen(s) by other donor atoms, such as O, S, Se and Te in a porphyrin ring leads to new macrocyclic systems referred to as core-modified porphyrins or heteroatom substituted porphyrins [2]. Such core perturbation affects the electronic structure of the ring system thereby altering the physical and chemical characteristics of the porphyrin macrocycle while retaining the aromatic character. Thus, the modification of the porphyrin core led to very interesting properties which are quite different from regular porphyrins. Specifically, the heteroporphyrins have the ability to stabilize metals in unusual oxidation states, such as copper in +1 and nickel in +1 oxidation states which are not possible to attain with regular porphyrins [3–11]. The heteroatom substituted porphyrins were first synthesized in 1969 [12–15] and for the last 35 years some elegant methodologies have been developed which resulted in much research activity on these porphyrin systems. However, until the late 1990s, most of the work on heteroporphyrins was limited to the preparation of different metal derivatives and the exploration of their structural, spectroscopic and electrochemical properties [3,4,6,9–11,16,18–24]. Latos-Grażyński, who is one of the pioneers in developing the heteroporphyrin chemistry has reviewed recently all the work that appeared on heteroporphyrins until

![Chart 1. The structures of 13 different mono- and diheteroporphyrins.](chart1.png)
1998 in “The Porphyrin Handbook” [2]. To the best of our knowledge, this is the only review on heteroporphyrins covering the synthetic aspects and discussing in detail the metalation studies, crystal structures, ground and excited state properties. However, during the last 5–6 years, there has been rapid development in heteroporphyrin chemistry with main emphases on synthesis of novel analogues of porphyrins, such as chlorins, carbaporphyrins, corroles, N- or X-confused porphyrins, β- and meso-substituted porphyrins and different covalent and non-covalent porphyrins arrays containing heteroatom substituted porphyrin units. The main objective of the present review is to provide an update on what has been achieved in the area of monoheteroatom substituted (21-N,X systems) and diheteroatom substituted porphyrin (21,23-N,X or 21,23-N2XY and 21,22-N2X2 or 21,22-N2XY systems) chemistry between 1999-February and 2005. This review is restricted to the developments occurred on heteroporphyrins containing four five-membered heterocyclic rings and does not include any discussion on heteroatom substituted expanded porphyrins containing more than four or five-membered heterocyclic rings which had been reviewed very recently [25,26]. Until now 13 different mono- and diheteroatom substituted porphyrins with various core combinations have been synthesized by replacing one or two nitrogen atoms of regular porphyrin (Chart 1)

Scheme 1. Synthetic routes for 21-monoheteroatom substituted porphyrins.
and this review discusses the developments with these systems (Chart 1). For setting the platform for review, in the first following two sections, we discuss very briefly the various synthetic approaches to obtain 21-hetero, 21,22 or 21,23-dihetero atom substituted porphyrins and their general properties. For detailed discussion on these two aspects, the interested reader is referred to Latos-Grażyński's article in "The Porphyrin Handbook" [2].

2. General synthetic strategies for mono- and diheteroatom substituted porphyrins

A few elegant methodologies have been developed over the years to synthesize mono- and diheteroatom substituted porphyrins which has been reviewed by Latos-Grażyński in "The Porphyrin Handbook" [2]. However, for continuity of the present review, we briefly summarize the various synthetic routes to synthesize the heteroatom substituted porphyrins containing one or two heteroatoms in the porphyrin core.

2.1. Synthetic routes for 21-monoheteroatom substituted porphyrins

To the best of our knowledge, there are five synthetic routes presently available to synthesize the 21-heteroatom substituted porphyrins as shown in Scheme 1. The first synthesis of 21-monoheteroatom substituted porphyrins was reported by Broadhurst et al. [12–15]. They adopted a [3 + 1] approach to synthesize 21-oxa-15 and 21-thia-16 porphyrins (Scheme 1a). The reaction of 2,5-diformylfuran 17 or thiophene 18 with tripyrrane diacid 19 generated in situ in the presence of HBr resulted in the formation of 21-oxa (25%) 15 or 21-thiaporphyrin 16 (12%), respectively. The Broadhurst approach was not found to be suitable for the synthesis of meso-tetraphenyl derivatives hence alternate methods have been developed using 2,5-bis(aryloxy)heterocyclopentadiene 20–23 as precursors [17,21,27–35]. One mole of the corresponding diol, 2,5-bis(aryloxy)heterocyclopentadiene 20–23 was condensed with two moles of arylaldehyde and three moles of pyrrole under Adler et al.'s [36] or Lindsey et al.'s [37] porphyrin forming conditions to give a mixture of three porphyrins and the required corresponding 21-heteroatom substituted porphyrins 2–5 which were separated from the mixture using column chromatography (Scheme 1b).

The 21-heteroatom substituted porphyrins 2–4 (X = S, O, Se) were also prepared by condensing the corresponding 2,5-bis(aryloxy)heterocyclopentadiene 20–22 with regular tripyrrane 24 in CH 3 CN under mild acidic conditions [31–33] (Scheme 1c). Recently, Chandrashekar and co-workers [34,35] have shown that the 21-oxa or 21-thiaporphyrins 3 can also be prepared by condensing the corresponding heterocyclopentadiene diols 20 or 21, respectively, with mesoaryl dipyrromethane 25 under mild acid catalyzed conditions (Scheme 1d). We recently developed a mono-ol method [38,39] to prepare 21-oxa and 21-thiaporphyrins (Scheme 1e). In this method, two equivalents of 2-(aryloxy)heterocyclopentadiene furan 26 or thiophene 27 were condensed with two equivalents of aryl aldehyde and three equivalents of pyrrole under Adler et al.'s or

Scheme 2. Synthetic routes for 21,23-diheteroatom substituted porphyrins.
Scheme 3. Synthetic routes for 21,22-diheteroatom substituted porphyrins.

Lindsey et al.’s conditions [36,37] resulting in a mixture of two porphyrins and the 21-oxa 2 or 21-thiaporphyrins 3 which were separated easily by column chromatography.

2.2. Synthetic routes for 21,23-diheteroatom substituted porphyrins

21,23-Diheteroatom substituted porphyrins were synthesized by following three different strategies. Broadhurst et al. [12–15] prepared the 21,23-diheteroatom substituted porphyrins 28–30 by acid catalyzed condensation of the 2,5-diformylfuran 17 or thiophene 18 with modified tripyrrane diacid 31 generated in situ (Scheme 2 a). This route gave access only to /H9252-meso-substituted meso-unsubstituted 21,23-diheteroporphyrins 28–30. Ulman and Manassen [27–30] developed two simple synthetic routes to prepare the meso-aryl substituted 21,23-diheteroporphyrins (Scheme 2 b and c). One equivalent of the corresponding heterocycle diol 20–22 was condensed with one equivalents of pyrrole under mild acid conditions followed by DDQ oxidation and this afforded 21,23-diheteroporphyrins having two similar heteroatoms 6–8. The mixed heteroatom substituted porphyrins 9–11 [28,29,31,32,35] were prepared by condensing one equivalent of the corresponding heterocyclopentadiene diols 20–23 with modified appropriate tripyrranes 32–34 under two step one flask room temperature conditions [37] (Scheme 2 c).

2.3. Synthetic routes for 21,22-diheteroatom substituted porphyrins

There are very few synthetic methods available to synthesize 21,22-diheteroatom substituted porphyrins [15,40,41]. Broadhurst and Grigg [15] synthesized the first 21,22-dioxa porphyrin 38 by [2 + 2] acid catalyzed condensation of a 5,5′-diformylfurlyl 36 with a dipyromethane diacid 37 (Scheme 3 a). Lee and Cho [40,41] recently developed a novel synthetic strategy to prepare 21,22-diheteroporphyrins 12–14 containing sulfur and oxygen atoms (Scheme 3 b).

The acid catalyzed condensation of one equivalent of 1,9-bis(phenylhydroxymethyl)-5-phenyldifuryl 38 or dithienyl 39 or furylthienylmethane 40 with one equivalent of 5-phenylpyrromethane 25b followed by oxidation with DDQ resulted in 21,22-diheteroporphyrins 12–14.

3. General properties of heteroporphyrins

The spectroscopic properties of heteroporphyrins indicate that they are aromatic and obey 4n + 2 π-electron Hückel rule [2]. The replacement of one or two nitrogen atoms with heteroatoms results in the alteration of π-delocalization, which in turn affects the electronic properties. Some of the salient features of the heteroporphyrins follow: (1) the alteration in π-delocalization due to heteroatoms results in considerable downfield shifts in 1H NMR of the pyrrole and heterocyclopentadiene moieties (Table 1). The deshielding was more for monoheteroatom substituted porphyrins than for diheteroatom substituted porphyrins [42,43]. This is attributed to the distortion of the porphyrin macrocycle by the two large heteroatoms, which decreases the ring current effect arising from the π-delocalization. (2) Similar to N₄ porphyrins, the heteroporphyrins shows an intense Soret band and 3–4 Q-bands in 700–450 nm region. The introduction of a heteroatom in place of “N” results in large red shifts of both Soret and Q-bands (Table 1). The maximum red shifts were observed with “S”, “Se” and “Te” containing heteroporphyrins [35,44] and the shifts were minimum for “O” containing heteroporphyrins [35,44]. Furthermore, the red shifts of the absorption bands of diheteroatom substituted porphyrins were greater than those of the monoheteroatom [35,44] substituted porphyrins. (3) The emission bands of the heteroporphyrins [35,44–46] were also red shifted with reduction in quantum yields compared to N₄ porphyrins (Table 1). The lifetimes of singlet excited state were generally very low except for oxaporphyrins whose lifetimes are almost comparable to those of N₄ porphyrins [35]. (4) The heteroatom porphyrins are easy to reduce and difficult to oxidize compared to regular porphyrins [35,47] (Table 1). This is attributed to the inductive or electron withdrawing effect...
<table>
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<tr>
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<th>$^1$H NMR</th>
<th>Electronic spectra, $\lambda_{max}$ (nm)</th>
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<th>X-ray distance (Å)</th>
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$^a$ X-ray data of porphyrin dication.
that the heteroatom has on the frontier orbital of the porphyrin. The heteroporphyrins also have a strong ability to stabilize metals in unusual oxidation states, which are not possible with regular porphyrins [2]. (5) The crystal structures solved for various heteroatom-substituted porphyrins and metalloporphyrins [2] indicate that the presence of large heteroatoms shrinks the core of mono- and diheteroporphyrins relative to those of regular porphyrins as revealed by the comparison of the diagonal of the tetragon formed by the donor atoms of the porphyrin core (Table 1). The variation of the structures of the heteroporphyrins compared to regular porphyrins alters the electronic properties considerably. However, the structures of oxaporphyrins are almost similar to those of regular porphyrins because of the similar sizes of the "N" and "O". Hence, the properties of oxaporphyrins are almost similar to that of N₄ porphyrins [35].

4. Latest developments in metal complexes of heteroporphyrins

It was well established that 21-monothia, 21-monooxa, 21-monoselena, 21,23-dioxa and 21-oxa-23-thiaporphyrins form metal complexes and the interesting features of the crystal structures solved for some of the metal complexes were discussed in detail in the Porphyrin Handbook [2]. Until recently, it was assumed that the 21,23-dithiaporphyrin did not form metal complexes which was attributed to the weaker coordinating ability of the thiophene moiety and also to its smaller core-size. However, Hung et al. [48] reported the synthesis and characterization of Ru(S₂TPP)Cl₂ (41), the first metal complex of 21,23-dithiaporphyrin (Chart 2). The 21,23-dithiaporphyrin was treated with five equivalents of Ru(COD)Cl₂ in o-dichlorobenzene at refluxing temperature followed by recrystallization yielded Ru(S₂TPP)Cl₂ in 52% yield. When other ruthenium metal sources, such as Ru₃(CO)₁₂ were used, metalation did not occur indicating that Ru(COD)Cl₂ is essential for the reaction. The absorption spectrum of 41 exhibited bathochromically shifted Soret (468 nm) and three Q-bands (563, 594 and 810 nm) and the bathochromic shifts were attributed to the distortion of the porphyrin ring.

The X-ray structure solved for 41 showed that both thiophene rings coordinate to ruthenium in a pyramidal side-on fashion and the geometry of sulfur resembles those of the thiaporphyrin and N₁-thiophene complexes (Fig. 1). The dithiaporphyrin ring was tilted away from the mean porphyrin plane. The pyrrole rings were planar with mean deviation of 0.038 Å, which was much smaller than the mean deviation of 0.373 Å observed for the thiophene rings. The chloride ions were tilted 26° from the normal of the mean plane and provide a regular octahedral co-ordinating geometry around the Ru(II) metal ion. The bond distances and bond angles around the dithiaporphyrin in 41 match closely with those of free base 21,23-dithiaporphyrin and this indicates that the ring distortion resulting from the insertion of large Ru(II) metal ion into the porphyrin ring did not affect the π-delocalization of the dithiaporphyrin. An electrochemical study of 41 showed the first oxidation at 0.35 V and the first reduction at −0.71 V which were assigned to Ru(II)/Ru(III) and Ru(II)/Ru(I) couple, respectively; however, it is more likely that the reduction process involves porphyrin reduction and not reduction to Ru(I).

Recently, three more metal complexes of 21-heteroporphyrins were reported [49–52]. Arnold and co-workers [49] prepared a lithium complex of 21-monothiaporphyrin 42 in 90% yield by reacting the porphyrin with lithium bis(trimethylsilyl)amide in THF at room temperature. The lithium complex 42 decomposes on exposure to even a slight trace of moisture. The absorption spectrum showed one strong Soret-like absorption at 458 nm along with a weaker broad
absorption at 346 nm and two Q-type absorption bands at 570 and 619 nm. The $^7$Li NMR showed a single peak at $-10.2$ ppm, which was at higher field compared to the dilithiated tetrarylporphyrins and supported that the lithium cation is bound in the centre of the macrocycle [49]. The X-ray analysis of 42 indicated that the macrocycle was distorted from planarity (Fig. 2).

The three pyrrolic subunits were almost planar and thiophene ring was out of plane with a dihedral angle of $12.5^\circ$ to the plane defined by the tripyrrane unit. The dihedral angle in 42 was smaller than that found for nickel(I)-21-thiaporphyrin complex ($14.6^\circ$) but larger than that of iron(II)-21-thiaporphyrin complex ($11.8^\circ$). The lithium cation was located 0.64 Å above the tripyrrane plane which was larger than that found for Ni(I)-21-thiaporphyrin complex (0.042 Å) and Fe(II)-21-thiaporphyrin complex (0.538 Å) [2]. The lithium ion in 42 was in a roughly square pyramidal arrangement with oxygen atom of the THF molecule occupying the fifth coordination site. The sulfur to lithium distance in 42 was comparable to those found in the corresponding Ni(I) {2.143(6) Å} and Fe(II) complexes {2.388(3) Å} of 21-thiaporphyrin [2] suggesting the presence of bonding interaction between these atoms.

Pawlicki and Latos-Grażyński synthesized the iron complexes of 21-oxaporphyrin [51,52]. The high spin six co-ordinate (OTPP)Fe(III)Cl$_2$ 44 was obtained in 63% yield by treating 21-oxaporphyrin with FeCl$_2$ in CHCl$_3$/CH$_3$OH followed by one electron oxidation with dioxygen [51]. The compound 44 was characterized by $^1$H NMR and single crystal X-ray analysis. The structure of 44 presented in Fig. 4 indicates that iron(III) ion is co-planar with the furan ring which coordinates the metal ion in $\eta^1$ fashion. The Fe$^{III}$-Cl(1) [2.302(1) Å] and Fe$^{III}$-Cl(2) [2.301(1) Å] distances in 44 were the longest found among the

![Fig. 2. X-ray structure of 42 (a) top view and (b) side view (reproduced with permission from Ref. [49]).](image)

![Fig. 3. X-ray structure of 43 (reproduced with permission from Ref. [50]).](image)

![Fig. 4. X-ray structure of 44 (a) top view and (b) side view (reproduced with permission from Ref. [51]).](image)
high-spin iron(III) porphyrins indicating the mutual *trans* interaction of axial chloride ligands.

The complex 44 was treated with mild reducing agents, such as sodium dithionite, which resulted in the formation of the one electron reduced product (OTPP)FeII Cl. When excess potassium cyanide was added to 44 in methanol, it resulted in the formation of low spin complex [(OTPP)FeIII(CN)2]. However, when this reaction was carried out under anaerobic conditions, the cyanide acts as a one electron reducing agent and produced the diamagnetic [(OTPP)Fe(CN)2]−. The (OTPP)FeII(CH2CH2CH2CH3) was obtained by reacting 44 or (OTPP)FeIICl with n-BuLi in n-hexane at 205 K. The (OTPP)FeII(CH2CH2CH2CH3) decomposed at 250 °C via homolytic cleavage of the iron–carbon bond and produced the low spin paramagnetic (OTPP)FeI.

5. Heteroporphyrin building blocks and covalent and non-covalent porphyrin systems

Although the general synthetic methods for heteroporphyrins have been well established, no attempts have been made to synthesize heteroporphyrins having functional groups at meso-positions. These could be useful to synthesize complex heteroporphyrin systems. Recently, a series of heteroporphyrin building blocks with porphyrin cores, such as N2S2, N3S, N1O and N2SO having 1–4 functional groups, such as iodo-, ethynyl-, hydroxy, aldehyde etc on meso-phenyls or pyridyl groups at meso-positions were synthesized [33,38,55,56]. These building blocks were used further to construct energy donor appended heteroporphyrin systems [56,58,63,64] and covalent [38,59,55,62] and non-covalent [59-61] unsymmetrical porphyrin arrays containing two dissimilar porphyrin cores.

5.1. Heteroporphyrin building blocks with four functional groups

The 21,23-dithiaporphyrin building blocks having four ethynyl, iodo and bromo functional groups on meso-phenyls 45a–d were reported recently [54,55,64]. The thiophene diols 46a–c were synthesized by reacting 2,5-dilithiothiophene with 4-bromobenzaldehyde, 4-iodobenzaldehyde and 4-trimethylsilylethynylbenzaldehyde, respectively, in THF (Scheme 4) under Ulman and Manassen conditions [30]. The porphyrins 45a–c were synthesized in 13–19% yields by condensing the respective diol 46a–c with pyrrole under mild acid porphyrin forming conditions (Scheme 5). The tetra-functionalized 21,23-dithiaporphyrin building blocks have been used to synthesize the covalently linked diaryl ethyne bridged boron-dipyrrin (BDPY) appended 21,23-dithiaporphyrin [55,63] (BDPY)4S2TPP 47 using copper free palladium(0) coupling conditions [65]. Coupling of 45d with

![Scheme 4. Synthesis of thiophene diols 46a–c.](image)

![Scheme 5. Synthesis of tetra-functionalized 21,23-dithiaporphyrins.](image)
Scheme 6. Synthesis of N₂S₂ porphyrin appended with four boron-dipyrrin appended units.

\[ \text{N,N-difluoroboryl-1,9-dimethyl-5-(4-iodophenyl)dipyrrin} \ 48 \] at 35 °C in the presence of a catalytic amount of Pd₂(dba)₃ and AsPh₃ followed by column chromatographic purification resulted in 20% yield (Scheme 6).

The \(^1^H\) NMR spectrum of 47 showed peaks corresponding to both porphyrin and boron-dipyrrin units with negligible changes in chemical shifts indicating little interaction between the units. The absorption spectrum of 47 showed one strong Soret and three Q-bands with almost no shifts in peak maxima confirming the weak interaction between the units. The photophysical properties of 47 were studied using both steady state and time-resolved fluorescence techniques [55,64,66]. The steady state fluorescence study carried out at 485 nm excitation wavelength where boron-dipyrrin units predominantly absorb, showed major emission from boron-dipyrrin units, indicated a very inefficient energy transfer from boron-dipyrrin units to 21,23-dithiaporphyrin unit (Fig. 5). The time resolved fluorescence study indicated that the rate of energy transfer in 47 from boron-dipyrrin unit to N₂S₂ porphyrin unit was slow [66]. The slow rate of energy transfer in 47 was attributed to the presence of two sulfur atoms in the porphyrin core, which increased the contribution of non-radiative decay channels. However, the similar boron-dipyrrin appended systems with regular porphyrin (BDPY)₄H₂TPP (the structure is not shown) reported earlier showed an efficient energy transfer (Fig. 5) from boron-dipyrrin unit to N₄ porphyrin unit [67].

The 21,23-dithiaporphyrin building block with four ethynylphenyl groups 45d was also used to synthesize the unsymmetrical porphyrin pentamer 49 containing one N₂S₂ unit and four N₄ units in 37% yield by coupling 45d with 5,10,15,20-tetra(3,5-di-tert-butylphenyl)porphyrin under similar copper free palladium coupling conditions (Chart 3) [54,55]. The Zn(II) derivative (ZnTPP)₂S₂TPP Zn₄9 (Chart 3) was prepared in 90% yield by treating 49 with Zn(OAc)₂ in CH₂Cl₂/CH₃OH under standard conditions [55]. The \(^1^H\) NMR and absorption studies indicated a weak interaction between the central N₂S₂ porphyrin unit and peripheral N₄ porphyrin units. The photophysical studies carried out at 420 nm for 49 where N₄ units absorbs strongly and at 550 nm for Zn₄9 where the zinc(II) derivative of N₄ unit is the dominant absorber indicated an efficient energy transfer from the peripheral N₄ or ZnN₄ porphyrin units to the central N₂S₂ porphyrin unit [54,55,64,66].

5.2. Heteroporphyrin building blocks with three functional groups

There are no reports available to synthesize the tri-functionalized heteroporphyrins prior to the recent mono-ol method developed by Gupta and Ravikanth, which gave access to the tri-functionalized 21-thia and 21-exoporphyrin building blocks [38,39]. Condensation of two equivalents of 2-(o-arylidenehydroxymethyl) thiophene 27 or furan 26 (thiophene or furan...
mono-ol) with two equivalents of functionalized aryl aldehyde and three equivalents of pyrrole under acid catalyzed conditions followed by column chromatography gave the desired tri-functionalized 21-thia or 21-oxaporphyrins (Scheme 7). By following this route, 21-thia 50a–d and 21-oxaporphyrins 51a–e containing three iodophenyl and pyridyl groups at the meso-positions were synthesized. Although this method gave low yields (2–6%), the trifunctionalized 21-thia and 21-oxaporphyrins can be prepared in good quantity using easily available precursors.

The use of the trifunctionalized heteroporphyrin building blocks was demonstrated by synthesizing two non-covalent unsymmetrical tetramers 52 and 53 containing one N=S and three N\textsubscript{4} porphyrin units (Chart 4) [39]. The non-covalent porphyrin

\[ \text{Chart 3. Diaryl ethyne bridged unsymmetrical covalent pentamers.} \]

\[ \text{Scheme 7. Synthesis of tri-functionalized 21-thia and 21-oxaporphyrins.} \]
arrays S2 and S3 were synthesized by treating porphyrin S0b and S0c, respectively, with RuTPP(CO)(EtOH) in toluene at refluxing temperature. Similar unsymmetrical tetramers were not formed when N3O porphyrin S1b or S1c were treated with RuTPP(CO)(EtOH) under identical reaction conditions.

The tetramer formation resulted in the large 1H NMR upfield shifts of inner NH, β-pyrrole and pyridyl protons of thiaporphyrin unit in S2 and S3 experienced about a ∼2 ppm upfield shift compared to their corresponding monomers. Similarly the pyridyl protons which were adjacent to RuTPP(CO) unit and β-pyrrole protons of thiaporphyrin unit in S2 and S3 also shifted upfield by ∼6 and ∼2 ppm, respectively, compared to their corresponding monomers.

### 5.3. Heteroporphyrin building blocks with two functional groups

Lindsay and co-workers [53] have developed a novel efficient method to prepare trans substituted 21-thia S4 and 21-oxaporphyrin S5 building blocks. Condensation of the functionalized thiopyrronmethane diol S6 or furylpyrromethane diol S7 with a functionalized dipyrromethane S8 under acid catalyzed conditions followed by column chromatography yielded S4 or S5 (Scheme 8) having iodophenyl and trimethylsilylthiophenyl/phenyl groups at the meso-positions in trans fashion. However, these compounds were not used in any applications.

A series of 21-thia and 21-oxaporphyrins with two functional groups at the meso-positions in cis fashion were synthesized [56-58,60] by condensing 2,2′-bis(α-aryl-α-hydroxymethyl)thiophene 21 or furan 20 with two equivalents of functionalized aryl aldehyde and three equivalents of pyrrole under porphyrin forming conditions (Scheme 9). This condensation resulted in the formation of a mixture of three porphyrins: a desired 21-thia S9 or 21-oxaporphyrin S60 along with 21,23-dithiaporphyrin S7 and regular porphyrin S1 which were separated by column chromatography. Using this approach the cis-porphyrin building blocks containing functional groups, such as iodophenyl, ethynylphenyl and pyridyl groups at the meso-positions were synthesized.

The 21-thia and 21-oxaporphyrin building blocks with two functional groups at the meso-positions in cis fashion were used to synthesize complex heteroporphyrin based systems. The covalently linked boron-dipyrrin appended 21-thia S61 and 21-oxaporphyrin S62 systems (Chart 5) were synthesized by coupling S9a and S60b respectively with 48 under copper free palladium coupling conditions [65]. The 1H NMR and absorption spectroscopic studies of S61 and S62 suggested a weak interaction between the boron-dipyrrin and porphyrin units. The photophysical properties were studied for S61 and S62 using static and time-resolved fluorescence techniques. The study indicated that both in S61 and S62, the energy transfer occurred from boron-dipyrrin units to 21-thia and 21-oxaporphyrin units, respectively. However, the rate of energy transfer in S62 was relatively faster than S61 which was attributed to the proximity of donor and acceptor units in S62 [64,66].

The cis-heteroporphyrin building blocks having meso-pyridyl functional groups were used to synthesize the non-covalent heteroporphyrin systems [59,60]. The non-covalent unsymmetrical trimers S63 and S64 (Chart 6) containing one

---

### Table 2

<table>
<thead>
<tr>
<th>Compound</th>
<th>Inner NH</th>
<th>2,6-Pyridyl</th>
<th>β-Pyrole</th>
</tr>
</thead>
<tbody>
<tr>
<td>S0b</td>
<td>−2.84</td>
<td>9.09 (m), 9.05 (s)</td>
<td>8.94 (s), 8.76 (d), 8.70 (d), 8.61 (d), 8.57 (d)</td>
</tr>
<tr>
<td>S2</td>
<td>−4.13</td>
<td>1.86 (d), 1.70 (t)</td>
<td>6.90 (m), 6.82 (m), 6.71 (d), 6.50 (d)</td>
</tr>
<tr>
<td>S0c</td>
<td>−2.74</td>
<td>9.44 (m), 9.04 (br s)</td>
<td>8.94 (s), 8.76 (d), 8.49 (d), 8.60 (s), 8.53 (m)</td>
</tr>
<tr>
<td>S3</td>
<td>−4.20</td>
<td>1.99 (m)</td>
<td>6.59 (m), 6.77 (m), 6.92 (m)</td>
</tr>
</tbody>
</table>

Chart 4. Unsymmetrical non-covalent porphyrin tetramers.

---

arrays S2 and S3 were synthesized by treating porphyrin S0b and S0c, respectively, with RuTPP(CO)(EtOH) in toluene at refluxing temperature. Similar unsymmetrical tetramers were not formed when N3O porphyrin S1b or S1c were treated with RuTPP(CO)(EtOH) under identical reaction conditions.

The tetramer formation resulted in the large 1H NMR upfield shifts of inner NH, β-pyrrole and pyridyl protons of 21-thiaporphyrin sub-unit in tetramers compared to the corresponding monomers (Table 2). The inner NH proton of the thiaporphyrin unit in S2 and S3 experienced about a ∼2 ppm upfield shift compared to their corresponding monomers. Similarly the pyridyl protons which were adjacent to RuTPP(CO) unit and β-pyrrole protons of thiaporphyrin unit in S2 and S3 also shifted upfield by ∼6 and ∼2 ppm, respectively, compared to their corresponding monomers.

### 5.3. Heteroporphyrin building blocks with two functional groups

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The cis-heteroporphyrin building blocks having meso-pyridyl functional groups were used to synthesize the non-covalent heteroporphyrin systems [59,60]. The non-covalent unsymmetrical trimers S63 and S64 (Chart 6) containing one
N_3S porphyrin core and two N_4 porphyrins cores were synthesized in 36–45% yields by treating cis-pyridyl porphyrins 59c and 59d, respectively, with RuTPP(CO)(EtOH) in toluene at refluxing temperature. The shifts of NH, β-pyrroles and pyridyl protons towards upfield compared to their corresponding meso-pyridyl porphyrin monomers in ^1H NMR confirmed the formation of trimers. The attempts to prepare the non-covalent trimers containing N_3O porphyrin 60c–d were not successful. Latos-Grażyński and co-workers [59] used the cis pyridyl N_3S porphyrin 59c to synthesize a self-assembled cyclic rhomboid dimer 65 (Chart 6) by treating 59c with 1,3-bis(diphenylphosphino)platinum bistriflate complex.

5.4. Heteroporphyrin building blocks with one functional group

Lindsey and co-workers [53] extended the same synthetic strategy, which they have used for the synthesis of trans-substituted core-modified porphyrin building blocks (shown in Scheme 8) to synthesize 21-thia and 21-oxaporphyrins with one functional group 66 and 67 (Chart 7). Condensation of the dipyrromethane 58b with thienylpyrromethane diol 56a and furylpyrromethane diol 57a resulted in the formation of mono-functionalized 21-thia 66 and 21-oxaporphyrin 67, respectively. By this method, 21-thia and 21-oxaporphyrins
containing a trimethylsilylthiophenyl functional group at meso-position adjacent to pyrrole ring were synthesized; the applications of these building blocks have not been explored [53].

Lee et al. [33] also prepared the mono-functionalized 21-thiaporphyrin 68 and 21-oxaporphyrin 69 by condensing the functionalized unsymmetrical tripyrrane 70 with symmetrical thiophene 27 or furan diol 26 under Lindsey’s conditions (Scheme 10). This condensation resulted in the formation of a mixture of three porphyrins and the required porphyrin 68 or 69 was separated by column chromatography. The method was used only to synthesize 21-thia and 21-oxaporphyrins containing an iodophenyl group at meso-position.

The mono-ol method which we have used to synthesize the tri-functionalized 21-thia and 21-oxaporphyrins was further extended to synthesize the mono-functionalized 21-thia 71a-d
Chart 7. 21-Thia and 21-oxaporphyrins having trimethylsilyl/ethynylphenyl functional group.

CH₃
H₃C
X N HN
Si(CH₃)₃
CH₃
X = S : 66
X = O : 67

Chart 8. N₄–N₃S₄ 81; N₃S–N₃O 82; N₃S–N₂S₂ 83; N₂S₂–N₃SO 84 were synthesized in decent yields under these coupling conditions [38,39,62]. NMR and absorption spectra of dimers 78–84 indicated a weak interaction between the porphyrin units. Since the porphyrins in unsymmetrical dimers

To synthesize the mono-functionalized 21-thiaporphyrins, one equivalent of diol 77 was condensed with two equivalents of aryl aldehyde and three equivalents of pyrrole under Lindsey or Adler’s conditions. This condensation gave a mixture of four porphyrins and the desired 21-thiaporphyrin 71 was separated by column chromatography. The mono-functionalized 21,23-dithiaporphyrin 75 were synthesized [62] by condensing the diol 77 with 16-thiatripyrane 33 (Scheme 12). The condensation resulted in the formation of mono-functionalized 21,23-dithiaporphyrin as sole product in 10–12% yields. The mono-functionalized 21-thia-23-oxaporphyrins 76 were prepared [62] as a single product by condensing diol 77 with 16-oxatripyrane 32 (Scheme 12).

The mono-functionalized porphyrin building blocks gave access for the first time to the unsymmetrical porphyrin dimers containing any two desired porphyrin units. We have explored the use of the mono-functionalized heteroporphyrins in the synthesis of a series of covalently linked unsymmetrical diaryl ethyne bridged porphyrin dimers 78–84 containing two different porphyrin cores [38,39,62]. The porphyrin dimers containing two different porphyrin cores were synthesized by coupling the appropriate porphyrin building block having the iodophenyl group with the porphyrin building block with ethynylphenyl group under Lindsey’s copper free mild palladium coupling conditions [65] as illustrated in Scheme 13 for the synthesis of 78. The dimer 78 was prepared by coupling of zinc(II) 5,10,15,20-tetakis(mesityl)porphyrin 85 with the deprotected form of 71a in the presence of Pd₂(dba)₃/AsPh₃ in toluene/triethylamine at 35 °C for 2 h (Scheme 13). Thus, a series of dimers containing different porphyrin cores (Chart 8), such as N₄–N₃S₄ 87–90. N₄–N₂S₂ 81; N₃S–N₃O 82; N₃S–N₂S₂ 83; N₂S₂–N₃SO 84 were synthesized in decent yields under these coupling conditions [38,39,62]. NMR and absorption spectra of dimers 78–84 indicated a weak interaction between the porphyrin units. Since the porphyrins in unsymmetrical dimers

Chart 10. Lee’s approach for the synthesis of mono-functionalized 21-thia or 21-oxaporphyrins.

78–84 absorb in two different regions, the photophysical properties of the dimers are expected to be interesting. A preliminary photophysical study was carried out on some of the unsymmetrical porphyrin dimers which exhibited interesting energy transfer properties from one porphyrin unit to the other on selective excitation of one porphyrin unit [39,62]. For example, a steady state fluorescence study of dimer 78 containing Zn(II) derivative of normal porphyrin and 21-thiaporphyrin sub-units was carried out with selective excitation at 550 nm where the Zn(II) derivative of normal porphyrin unit absorbs strongly. The major emission was observed from the 21-thiaporphyrin unit suggesting an efficient energy transfer from the Zn(II) derivative of the normal porphyrin unit to the 21-thiaporphyrin unit (Fig. 6). Similarly, the dimers 79–81 also showed an efficient energy transfer from donor porphyrin unit (normal porphyrin or its zinc(II) derivative) to acceptor porphyrin unit (21-thia, 21-oxa and 21,23-dithiaporphyrins) as confirmed by steady state fluorescence studies [39,62].

The mono-functionalized heteroporphyrins having pyridyl functional groups at meso-positions were used to synthesize unsymmetrical non-covalent porphyrin dimers 86–89 (Chart 9). The 21-thia 71f, g and 21,23-dithiaporphyrin 75e, f building blocks were reacted with RuTPP(CO)(EtOH) in toluene overnight and afforded dimers 86–89 (Chart 9) in decent yields [61,68].

6. β-Substituted heteroporphyrins

Porphyrins have two reactive positions—the β- and meso-positions at which suitable substituent(s) can be introduced to tune the electronic properties of the porphyrin for specific applications. The β-functionalization of porphyrins is of considerable chemical interest since the β-substituents are in direct conjugation with the porphyrin ring and small changes in the substituents alter the properties of the porphyrin macrocycle. There are several reports on both electron releasing and electron withdrawing substituents at β-pyrrole carbons of regular porphyrin systems [69,70]. Porphyrins with electron withdrawing substituents, such as –Br, NO₂ at β-pyrrole carbons of regular porphyrins are found to be robust catalysts for alkene epoxidation and alkane hydroxylation reactions [71,72,73]. However, until recently, there are no reports on β-substituted heteroporphyrins to understand the β-substituent effects on electronic properties of heteroporphyrins. Recently, a series of 21-thia and 21,23-dithiaporphyrins having bulky substituents at β-positions have been synthesized [74–79]. Both β-pyrrole [74,78] and β-thiophene substituted thiaporphyrins [73–77,79] have been synthesized and the spectroscopic properties were studied.
6.1. β-Pyrole substituted thiaporphyrins

We synthesized three β-pyrole substituted 21,23-dithiaporphyrins by following the known synthetic methodologies (Chart 10). The tetrabrominated 21,23-dithiaporphyrin 90a was synthesized in 70% yield by treating 7 with 4.2 equivalents of N-bromosuccinimide in chloroform at refluxing temperature. The bromines at the β-pyrole carbon atoms of the thiaporphyrin 90a resulted in upfield shifts of 0.26 ppm of the β-thiophene protons in 1H NMR and red shifts of absorption and emission bands compared to 7 [74]. Unsuccessful attempts were made to use 90a as a precursor to synthesize the β-aryl substituted thiaporphyrins by treating 90a with different aryl boronic acids under Suzuki coupling conditions. However, the aryl substituted 21,23-dithiaporphyrins 90b and 90c (Chart 10) were obtained by condensing the corresponding 3,4-disubstituted pyrroles 91a,b with thiophene diol 21 under mild acid conditions (Scheme 14) [74].

The large upfield shifts of the β-thiophene protons (0.44 ppm) in 1H NMR and more red shifts in absorption and emission bands of 90b compared to 7 (Table 3) indicated that the presence of bulky phenyl groups at the β-pyrole carbon atoms alter the electronic properties of the porphyrin more drastically.

6.2. β-Thiophene substituted thiaporphyrins

We synthesized a series of β-thiophene substituted 21,23-dithiaporphyrins [75–77,79]. The 21,23-dithia 92a–d and 21-thiaporphyrins 93a–d having methyl and phenyl groups at β-thiophenes were synthesized by condensing the appropriate 3,4-disubstituted thiophene diols 94a–d with pyrrole and with aryl aldehyde and pyrrole, respectively, under standard acid catalyzed conditions (Scheme 15). Spectroscopic studies on β-thiophene substituted thiaporphyrins showed the upfield shifts in 1H NMR, red shifts in absorption and emission bands compared to the β-unsubstituted thiaporphyrins (Table 3). Furthermore, the magnitude of spectroscopic shifts were directly related to the number of β-substituents (Table 3).

A series of cyclic substituents, such as propane-1,3-diyldioxy and its ethyl and benzyl derivatives substituted at the β-thiophene carbon atoms of 21,23-dithiaporphyrins 95a–c and 21-monothiaporphyrins 96a–c were synthesized (Scheme 16) [77]. 21,23-Dithiaporphyrins 95a–c were prepared in 8–12% yields by condensing the substituted appropriate thiophene diols 97a–c with pyrrole and 21-monothiaporphyrins 96a–c were prepared in 7–9% yields by condensing the substituted thiophene diols with benzaldehyde and pyrrole under standard conditions (Scheme 16). The cyclic substituents introduced at the β-thiophene carbon atoms alter the electronic properties of the porphyrins moderately (Table 3). The moderate changes in the

Table 3
Selected spectroscopic data of \(\beta\)-thiophene and \(\beta\)-pyrrole substituted thiaporphyrins

<table>
<thead>
<tr>
<th>Compound</th>
<th>(\beta)-Thiophene/(\beta)-furan (ppm)</th>
<th>(\beta)-Pyrrole (ppm)</th>
<th>Absorption</th>
<th>Emission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Soret (nm)</td>
<td>Q-band (nm)</td>
<td>(\lambda_{em}) (nm)</td>
<td>(\phi)</td>
</tr>
<tr>
<td>7</td>
<td>9.68 (s)</td>
<td>8.67 (s)</td>
<td>435</td>
<td>696</td>
</tr>
<tr>
<td>90b</td>
<td>9.23 (s)</td>
<td>–</td>
<td>440</td>
<td>700</td>
</tr>
<tr>
<td>92d</td>
<td>–</td>
<td>8.10 (s)</td>
<td>443</td>
<td>708</td>
</tr>
<tr>
<td>95c</td>
<td>–</td>
<td>8.39 (s)</td>
<td>446</td>
<td>714</td>
</tr>
<tr>
<td>98d</td>
<td>–</td>
<td>8.26 (s)</td>
<td>441</td>
<td>705</td>
</tr>
<tr>
<td>3</td>
<td>9.81 (s)</td>
<td>8.61 (d), 8.72 (d), 8.88 (s)</td>
<td>429</td>
<td>673</td>
</tr>
<tr>
<td>93d</td>
<td>–</td>
<td>8.32 (s), 8.45 (q), 8.88 (s)</td>
<td>448</td>
<td>705</td>
</tr>
<tr>
<td>96c</td>
<td>–</td>
<td>8.49 (s), 8.83 (q)</td>
<td>432</td>
<td>680</td>
</tr>
<tr>
<td>99a</td>
<td>–</td>
<td>8.45 (d), 8.52 (d), 8.87 (m)</td>
<td>430</td>
<td>678</td>
</tr>
<tr>
<td>99d</td>
<td>–</td>
<td>8.42 (s), 8.50 (d), 8.84 (d)</td>
<td>431</td>
<td>678</td>
</tr>
</tbody>
</table>

spectroscopic properties of the porphyrins were due to the flexible nature of the cyclic substituents at the β-thiophene carbon atoms.

The crystal structure solved for 96c showed it is more planar [77] (Fig. 8) than the slightly saddle shaped β-unsubstituted 21-N3SP 3b [80] which was reflected in their dihedral angles. The dihedral angles between the plane of the meso-carbon atoms and the four five-membered rings of 96c and 3b, respectively, are: thiophene, 2.6° and 14.1°; pyrrole N(1), 4.9° and −11.5°; N(2), 5.6° and 10.0°; N(3), 0° and −7.4°. The non-bonded N(1)⋯N(3) distance in 96c was almost the same as that of 3b but the non-bonded S⋯N(2) distance in 96c was slightly lower compared to 3b. The C9⋯S, C10⋯C12 and C11⋯C13 bond lengths of both the pyrrole and thiophene rings of 96c were slightly altered compared with 3b indicating that the π-delocalization was altered in the porphyrin macrocycle due to the presence of the substituent at the β-thiophene carbon atoms.

A series of tetraalkoxy and dialkoxy substituted 21,23-dithiaporphyrins 98a–d and 21-monothiaporphyrins 99a–d.
Scheme 17. Synthesis of β-thiophene substituted thiaporphyrins with alkoxy substituents.

respectively, having methoxy, butoxy, octyloxy and dodecyloxy substituents at β-thiophene carbon atoms [75,79]. These porphyrins, were synthesized by using appropriate alkoxy substituted thiophene diols 100a–d as shown in Scheme 17.

The presence of alkoxy substituents at β-thiophenes resulted in shifts in 1H NMR and red shifts of absorption and fluorescence bands compared to their unsubstituted 7 and 3 porphyrins (Table 3). The structures of 98b (Fig. 9) and 99a (Fig. 10) were elucidated by single crystal X-ray diffraction analysis [75,79]. Interestingly, 98b was more planar compared to 7 [80] suggesting that the presence of butoxy substituents at the β-thiophene carbon atoms induced more planarity. The four five-membered rings in 98b were in the same plane with four meso-carbons with negligible deviation unlike 7 in which the four five-membered rings slightly deviated from the plane of the four meso-carbons [80]. The non-bonded S···S′ and the N···N′ distances were slightly increased and decreased, respectively, in 98b compared to 7. The presence of substituents at β-thiophene 98b also resulted in the decrease of the Cα–Cβ and Cβ–Cβ distances of the thiophene rings in 98b compared to 7. The structure of 99a (Fig. 10) was slightly saddle-shaped with a mean deviation of 0.16 Å for the atoms in the porphyrin core. This was similar to that of β-unsubstituted porphyrin 3b [80] suggesting that the two methoxy groups at β-thiophene carbon atoms in 99a did not influence the structure of the porphyrin. In 99a, one of the methoxy groups on the β-thiophene carbon tilted upward and the other methoxy group was tilted downward [79]. The Cα–S, Cβ–Cβ distances in 99a were almost similar to that of 3b.

7. meso-Substituted heteroporphyrins

Porphyrin macrocycles are synthetically very flexible and by introducing substituents at β- or meso-positions, the properties can be tuned at will for any application. Most of the porphyrins and heteroporphyrins reported to date commonly have six-membered aryl groups at meso-positions. Recently, regular porphyrins having meso-substituents as five-membered heterocycles, such as thiophene [81–85] exhibited very interesting spectroscopic and electrochemical properties, which were attributed to the strong interaction between the porphyrin macrocycle and the five-membered meso-substituents. The interesting electronic properties of the porphyrins with five-membered heterocycles as meso-substituents suggests that these porphyrins...
can be used as a substitute for meso-tetraarylporphyrins for various applications. We synthesized a series of heteroporphyrins having 2-furyl, 2-thienyl and 3-thienyl groups at the meso-positions and studied their ground and excited state properties [86–90]. The heteroporphyrins having two and four furyl groups at meso-positions were synthesized using 2,5-bis(2-furylhydroxymethyl)thiophene \(101\) or furan \(102\). The tetrafuryl substituted 21,23-dithiaporphyrin \(103\) was prepared by condensing the diol \(101\) with pyrrole and the tetrasubstituted 21-thiaporphyrin \(104\) was prepared (Scheme 18) by condensing the same diol \(101\) with furan-2-carboxaldehyde and pyrrole under standard conditions [86]. The difuryl substituted 21-thiaporphyrins \(105\) and 21-oxaporphyrins \(106\) were prepared (Scheme 18) by condensing \(101\) and \(102\) respectively with \(p\)-tolylaldehyde and pyrrole under mild acid catalyzed conditions [86,87]. The introduction of five-membered furyl groups at meso-positions of heteroporphyrins altered the electronic properties drastically compared to the heteroporphyrins with six-membered aryl groups. This was reflected in the downfield shifts of the pyrrole and thiophene protons in \(^1\)H NMR and red shifts of absorption and emission bands with reduction in intensity and lifetimes of singlet excited states of meso-furyl porphyrins [87] compared to meso-aryl analogues (Table 4). The changes in the spectroscopic properties were attributed to the greater resonance interaction between the porphyrin and five-membered heterocycles [87,89].

We also synthesized meso-thienyl substituted porphyrins with different cores, such as N\(_3\)S, N\(_3\)O and N\(_2\)S\(_2\) [88]. The meso-2-thienyl substituted 21,23-dithiaporphyrin \(111\) and 21-thiaporphyrins \(112a\), \(b\) were prepared using diol \(107\) and meso-2-thienyl substituted 21-oxaporphyrins \(113a\), \(b\) were prepared using diol \(108\) under standard conditions (Chart 11). The heteroporphyrins \(114–116\) with two and four 3-thienyl groups at meso-positions were synthesized using diols \(109\) and \(110\) (Chart 11). Similar to meso-furyl heteroporphyrins, the meso-thienyl heteroporphyrins also exhibited changes in \(^1\)H NMR, absorption and emission properties [88,90] (Table 4). However, the effects observed for meso-thienyl heteroporphyrrins were comparatively less in magnitude than meso-furyl heteroporphyrins (Table 4).

The X-ray structures were solved for meso-thienyl heteroporphyrins \(111\) and \(115\) [88]. The structure of \(111\) was almost
planar (Fig. 11). The four five-membered rings were in the same plane as the four meso-carbon atoms with negligible deviation from planarity and the meso-thienyl substituents were out of the plane of porphyrin. Two of the meso-thienyl sulfur atoms were above the plane and other two were below the plane. The non-bonding N···N’ (4.61 Å) and S···S’ distances (3.058 Å) were shorter in 111 than in 7 (N···N’: 4.65 Å, S···S’: 3.069 Å) [80], indicating that 111 is more planar than 7. The C₆-C₆ distances of thiophene and pyrrole rings in 111 [1.353(5) and 1.3331(6) Å, respectively] were significantly shorter than in 7 [80], due to the altered π-delocalization in 111 because of the thienyl substituents at the meso-positions. The most novel feature of 111 was the observation of intermolecular hydrogen bonding holding the porphyrin rings in a supramolecular array formed due to the presence of a C≡H−N hydrogen bond between the meso-thienyl CH group of one porphyrin ring and the pyrrole N atom of another porphyrin [88]. This H-bonding was limited to the single strand to form a ladder-type supramolecular assembly and was not extended between the strands. The structure of 21-thiaporphyrin 115 (Fig. 12) with two meso-thienyl groups and two meso-aryl groups [88] was planar (Fig. 12) compared to the saddle-shaped structure of 3b [80]. In 115, the non-bonding N(1)···N(3) distance (4.392 Å) was almost the same as that of 3b but the non-bonding S···N(2) distance (3.570 Å) was longer than 3b (3.547 Å) supporting the planarity observed for 115.

Porphyrins having bulky dendritic wedges at the meso-positions have received a lot of attention in recent years because of their importance as biomimic models [91,92], for catalytic applications [93] and also as attractive building blocks for the formation of supramolecular architectures having well defined shapes and dimensions [94,95]. However, to date there is only one report on heteroporphyrs having phenyl ether based second generation dendrons at meso-positions [96]. The 21-oxaporphyrin 117 (Scheme 19) having a bulky phenyl ether based second generation dendron at two meso-positions in cis fashion was synthesized in 4.6% yield by condensing furan diol 20 with a second generation dendritic aldehyde 118 and pyrrole in propionic acid at refluxing temperature [96].

The emission study showed an energy transfer from dendritic wedges to porphyrin unit. The material properties of 117 and its Cu(II) derivative Cu117 were studied by optical microscopy and AFM analysis in contact mode. The optical microscopy of 100 μM solutions of the Cu(II) derivative of 2 (CuOTPPC) showed random aggregates but Cu117 showed the formation of large and small spherical aggregates up to 7.5 μm size [96]. The AFM analysis supported the formation of large spherical structures of Cu117 and showed that the Cu117 formed nearly spherical, robust and isolated assemblies whereas CuOTPPC formed random aggregates on a glass surface (Fig. 13). This study suggested that the dendritic wedges assist in the formation of large spherical supra structures with well-defined dimensions.
meso-Unsubstituted heteroporphyrins

Porphyrins with meso-unsubstituted carbon(s) played a vital role in synthetic porphyrin chemistry. The high reactivity of the meso-carbon bridge of the meso-unsubstituted porphyrins made these porphyrins ideal precursors for the synthesis of more complex systems with special physical and chemical properties. The β-unsubstituted meso-unsubstituted porphyrin or porphin, has not been well studied because of its very poor solubility characteristics. Broadhurst and Grigg [15] in the early 1970s synthesized 21-monoheteroporphyrins 15 and 16 as well as 21,23-diheteroporphyrins 28–30 with four meso-unsubstituted carbons (Schemes 1a and 2a). Chmielewski et al. reported the synthesis of 21-oxaporphyrin with one meso-unsubstituted carbon but its chemistry was not extended further [2,9]. We recently reported the synthesis of a series of thiaporphyrins with four, and two meso-unsubstituted carbons (Chart 12) using simple thiophene diols [97,98]. The synthesis of 21,23-dithiaporphyrin 120 with four meso-unsubstituted carbon atoms as well as β-unsubstituted carbon atoms was attempted using thiophene diol 119. However, the compound was not isolated due to the
Chart 12. Four and two meso-unsubstituted thiaporphyrins and their precursor diols.

unstable nature of the porphyrin. The four meso-unsubstituted but β-substituted 21,23-dithiaporphyrin 122 and two meso-unsubstituted 21-thiaporphyrin 123 were synthesized using thiophene diol 121. Similarly, the thiophene diol 124 was used to synthesize the four meso-unsubstituted 21,23-dithiaporphyrin 125 and two meso-unsubstituted 21-thiaporphyrin 126. The crystal structure solved for 126 exhibited the formation of a supramolecular assembly [98] due to intermolecular C–H···O and C–H···N hydrogen bonded interactions (Fig. 14).

A series of mono meso-unsubstituted heteroporphyrins with different cores, such as N2S, N2O, N3S2, N3O2, N2SO and N2OS [127–132] were synthesized [99] by following three different strategies (Scheme 20). The mono meso-unsubstituted 21-thiaporphyrin 127 and 21-oxaporphyrin 128 were synthesized by condensing the unsymmetrical thiophene diol 133 and furan diol 134, respectively, with aldehyde and pyrrole (Scheme 20a). The mono meso-unsubstituted 21,23-dithiaporphyrin 129, 21,23-dioxaporphyrin 130, 21-thia-23-oxaporphyrin 131 and 21-oxa-23-thiaporphyrin 132 were prepared by condensing appropriate unsymmetrical diols (133 and 134) and symmetric tripyrranes (33b and 32b) as shown in Scheme 20b. The mono-meso-unsubstituted 21-thia-23-oxaporphyrin 131 and 21-oxa-23-thiaporphyrin 132 were also prepared alternately as presented in Scheme 20c by condensing the corresponding unsymmetrical tripyrrane (135 and 136) with an appropriate symmetrical diol (20b and 21b).

The reactivity of meso-unsubstituted porphyrins was tested towards electrophilic and nucleophilic substitution reactions. The dibromo derivative 137 was synthesized in 55% yield by treating porphyrin 126 with N-bromosuccinimide in CHCl₃ at room temperature [98]. The diethynyl porphyrin 138 was synthesized in 58% yield by treating 137 with trimethylsilylacetylene in the presence of catalytic amounts of PdCl₂(PPh₃)₂/Cul in THF/triethylamine followed by deprotection of the trimethylsilyl group with K₂CO₃ in THF/CH₃OH (Scheme 21).

The meso-bis(palladio)porphyrin 139 was synthesized [98] in 28% yield under Arnold et al. [100] conditions by treating 137 with Pd₂(dba)₃/PPh₃ in toluene at room temperature (Scheme 21). The meso-butyl porphyrin 140 was synthesized using Kalisch and Senge method [101] by treating porphyrin 127 with n-BuLi at 0 °C in THF followed by oxidation with DDQ (Scheme 22). The mono bromo derivative 141 was synthesized similarly by treating 127 with N-bromosuccinimide in CHCl₃ at room temperature which was then coupled with 71a under palladium...
coupling conditions to yield the symmetrical covalently linked phenylethyne bridged dimer 142 containing two N$_2$S porphyrin cores (Scheme 23).

9. Heteroatom substituted corroles, carbaporphyrins, chlorins, bacteriochlorins and tetrabenzoporphyrins

9.1. Heterocorroles

A corrole molecule is an 18 π-electron aromatic tetrapyrrole macrocycle with a direct α–α pyrrole–pyrrole link. Since corroles have three ionisable hydrogen atoms, these molecules can stabilize metals in +3 oxidation state whereas porphyrins, which have two ionisable hydrogen atoms tend to stabilize only +2 metal ions. Hence, much attention has been directed recently on corrole chemistry [102,103]. Johnson and Kay [104,105] were the first to report the synthesis of 1-alkylated 21,23-dioxacorrole, 21-oxacorrole and 22-oxacorrole by ring closure reaction of the corresponding heteroatom containing metallo linear tetrapyrroles. Later, Broadhurst et al. [106,107] synthesized a variety of heteroatom containing metallocorroles by 2 + 2 Macdonald type of condensation of dipyrromethanes and 2,2'-bifuran or 2,2'-bithiophene at elevated temperatures. The first synthesis of core-modified meso-aryl corrole was reported by Chandrashekar and co-workers [108]. They isolated 5,10,15-triaryl-21-oxacorrole 143 as a byproduct in 8%
yield in their attempts to synthesize oxa-smaragdyrin 144 by an acid catalyzed oxidative coupling reaction of 32a and meso-phenyl dipyrromethane 25 (Scheme 24). Since 143 was formed in acid, the formation of 143 was attributed to the acidolysis of dipyrromethanes followed by the recombination of fragmented products [108].

NMR studies revealed that 143 exhibits asymmetric tautomerism where the NH proton adjacent to the furan ring was localized and the other NH proton on the bipyrrolic unit was changing sites between the two nitrogen atoms of the bipyrrolic unit. The 21-oxacorrole 143 showed usual intense Soret and four Q-bands in the visible region. On protonation, the Soret band split due to the lowering of symmetry. The emission spectrum of 143 was blue shifted compared to 2 with a high quantum yield (0.88) relative to 2 (0.075). Interestingly, even the protonated species of 143 was highly emitting with a quantum yield of 0.23. The X-ray structure of 143 (Fig. 15) exhibited an almost planar structure with only a small deviation of the inner-core heteroatoms from planarity varying from 5.48° to 7.74° [109]. The planarity of 143 was attributed to less steric hindrance in the macrocycle because of the presence of only two hydrogen atoms unlike regular corroles which showed small deviations from planarity due to three inner hydrogen atoms causing strain in the macrocycle. Furthermore, 143...
showed columnar structures due to \( \pi - \pi \) interactions between the macrocycles. A variety of metal complexes of 143 have been investigated [109]. Since 143 is a dianionic ligand, it stabilizes metals in the +2 oxidation state provided that all the heteroatoms in the core participate in the coordination. Four metal derivatives (Rh, Cu, Ni and Co) of 143 were prepared by reacting 143 with appropriate metal precursors [109]. 143 stabilizes Ni, Cu, Co in +2 oxidation states with the participation of all heteroatoms in the coordination. However, 143 stabilizes Rh in the +1 oxidation state since it binds to only two heteroatoms of the macrocycle. These observations were in contrast with corroles that act as trianionic ligands favoring higher oxidation states. The metal insertion into 143 was found to be difficult compared to normal corroles. The crystal structures of Rh(I) and Ni(II) complexes of 143 were analyzed [109]. The Rh(I) complex of 143 was non-planar and the Rh(I) ion was located above the corrole plane (Fig. 16). Rh(I) binds to only one imino and one amino nitrogen of the macrocycle and the other two coordination sites were occupied by carbonyl ligands providing square planar geometry around the Rh(I) ion. This type of coordination was preferred by Rh(I) possibly to avoid strain in the macrocycle. The Ni(II) complex of 143 is almost planar with a distorted square planar geometry around the Ni(II) ion (Fig. 17). The Ni(II) ion lies above the mean plane of the macrocycle by only 0.008 Å and acquired distorted square planar geometry around the metal ion. The comparison of Ni–N and Ni–O distances of 143 with that of corresponding Ni(II) derivative of 2 [9] showed that in 143 the bond distances were much shorter reflecting the reduced core size in Ni(II) 143.
Fig. 15. X-ray structure of 143 (a) top view and (b) side view (reproduced with permission from Ref. [109]).

Fig. 16. X-ray structure of Rh(I)143 (reproduced with permission from Ref. [109]).
Fig. 17. X-ray structure of Ni(II)143 (a) top view and (b) side view (reproduced with permission from Ref. [109]).

The absorption spectra of metal derivatives showed the characteristic Soret type and Q-type bands in the 400–700 nm region. The presence of inner NH (δ = −1.15) in NMR of Rh(I)143 supported the coordination of Rh(I) ion to only two nitrogen atoms. The NMR studies also showed the diamagnetic nature of Ni(II)143 which was in contrast with paramagnetic Ni(II) derivative of 2 [9]. Electrochemical studies on 143 and its metal complexes indicated that 143 and its metal complexes were easier to oxidize and harder to reduce compared with the corresponding porphyrin derivatives. Surprisingly, the metal derivatives of 143 did not show their characteristic metal reductions unlike corresponding metalloporphyrins [2].

Chandrashekar and co-workers further extended their work on 21-oxacorroles and synthesized 21-oxacorroles with one meso-free carbon 144 by three different routes [110,111]. The “3 + 1” condensation of 32 with 2-pyrole carboxaldehyde in the presence of trifluoroacetic acid in CH2Cl2 followed by oxidation with p-chloranil (Scheme 25) gave the 21-oxacorroles with one meso-free carbon in 9–15% yield depending on the concentration of acid catalyst used (Scheme 25a). Alternately, 144 was also prepared in 13–15% yield by condensing 32 with pyrrole and para-formaldehyde or formalin in the presence of 0.5 equivalent of TFA followed by oxidation with p-chloranil (Scheme 25b). The 21-oxacorrole 144 was also prepared by condensing 32 with 2-(hydroxyphenylmethyl)pyrrole under the same acid catalyzed conditions (Scheme 25c). In all three methods, both condensation and oxidative coupling reactions
Scheme 26. Synthesis of 21-oxacorrole and 22-oxacorrole by 2 + 2 condensation of two different regio-isomers of dipyrromethane with ferrocene moiety as well as the non-planarity of the corrole ring. The electronic coupling between the corrole and ferrocene moiety and the oxacorrole conjugates.

Chart 13. meso-Ferrocenyl dipyrromethane and ferrocenyl-21-oxacorrole conjugates.

takes place simultaneously. Chandra and co-workers used the same strategy and synthesized the ferrocenyl-oxacorrole conjugates 145 (Chart 13) by condensation of the meso-ferrocenyl dipyrromethane 146 with various para-substituted 5,10-diphenyl-16-oxatripyrranes 32 under acid catalyzed conditions [112].

The electronic spectra of 145 showed that the ferrocene substitution at the meso-position resulted in the shift of both the Soret and Q-bands relative to oxacorrole 143 indicating the presence of a strong electronic interaction between the ferrocene moiety and the oxacorrole π-system [112]. Electrochemical studies of 145 showed three quasi-reversible oxidations of (ΔEo = 70–130 mV) of which one was based on the ferrocene and the other two were on the corrole ring. The corrole ring oxidations in 145 were shifted to more positive potentials compared with 143, which was attributed to the combined effect of electronic coupling between the corrole π-system and the ferrocene moiety as well as the non-planarity of the corrole ring. The corrole ring reductions in 145 were shifted towards less negative potentials compared with 143 due to the electron deficient nature of corrole ring in 145 [112].

Cho and Lee [113,114] adopted a “2 + 2” methodology of acid catalyzed condensation of two different regio-isomers of furylypyrromethane alcohols 147 and 148 with dipyrromethane 25b and synthesized 21-oxacorrole 143 and 22-oxacorrole 149, respectively, bearing an oxygen atom at the designated site (Scheme 26). The absorption spectra of 143 and 149 have distinctly different features [114]. The Soret and Q-bands of 143 were more red shifted compared with 149. The blue shifted absorption bands of 149 indicated that it was less flexible and more resonance stabilized than 143. The 1H NMR spectroscopic analysis was also in agreement with this assumption. The β-pyrrolic protons and inner NH protons in 1H NMR of 149 were shifted more downfield and upfield, respectively, compared with the corresponding protons of 143 supporting the view that 149 was more resonance stabilized.

Latos-Grażyński and co-workers [115] reported the synthesis 21,23-dioxacorrole 150 in 8% yield by condensing 20, 26 and pyrrole under acid catalyzed conditions (Scheme 27). The use of 26 was essential for the creation of direct pyrrole-furan α-α bond to form 150. The UV–visible spectrum of 150 showed a corrole-like spectrum with split Soret band (397 and 422 nm) and the C–C distances were longer and shorter, respectively, in the corrole macrocycle than in free furan indicated the π-delocalization the furan ring was altered in 150. The nickel(II) complex of 150 is high spin (paramagnetic) and five coordinate [115] unlike the Ni(II) complex of 143 which was diamagnetic [109]. They have also synthesized the non-aromatic isomer of 150 with a protruding furan ring 152 by condensing 3-phenylhydroxymethylfuran 151 in place of 26 with 20 and pyrrole under similar reaction conditions (Scheme 27) [115]. In this reaction, instead of the expected isomer 153, the isomer with protruding furan ring 152 was formed because the condensation took place only at the sterically hindered β-position and not at the expected α-position. The UV–visible and 1H NMR spectra confirmed the non-aromatic nature of the macrocycle. The crystal structure of protonated species [152-HCl] (Fig. 19) showed that the macrocycle was...
Fig. 18. X-ray structure of 150, top view (reproduced with permission from Ref. [115]).

strongly puckered [115]. The chloride anion was located over the centre of the macrocycle and was involved in two intramolecular NH – Cl and two intermolecular (C)H – Cl interactions. The protruded furan ring preserved all features of the isolated furan and bond lengths were identical to that of free furan. However, the bond lengths of the second furan moiety were altered indicating appreciable π-delocalization in the second furan ring [115].

9.2. Heterocarbaporphyrins

Carbaporphinoids, which are porphyrin analogues where one or more of the pyrrole units have been replaced by carbo cyclic rings received much attention in the mid 1990s. Lash carried out extensive work on carbaporphyrins and explored their unusual physico-chemical properties [116-120]. The carbaporphyrins were mainly synthesized through a [3 + 1] acid catalyzed MacDonald type condensation reaction of appropriate precursors. Lash and co-workers have shown that these carbaporphyrins form very interesting stable organometallic derivatives with a range of metals, such as Pd(II), Pt(II) and Ag(III) to name a few [121-129]. The chemistry of carbaporphyrins has been reviewed recently by Lash in “The Porphyrin Handbook” [130]. The first examples of carbaporphyrins containing heteroatoms, such as S and O in addition to pyrrole nitrogen atoms were synthesized [131] by following their well-established 3 + 1 synthetic strategy used for the synthesis of the aza carbaporphyrins [130]. They attempted to synthesize the thia azuliporphyrin 154, selena azuliporphyrin 155 and oxa azuliporphyrin 156 using a novel tripyrrane 157 (Scheme 28) [131,132].

Fig. 19. X-ray structure of (152-H)Cl. (a) Top view and (b) side view (reproduced with permission from Ref. [115]).
The tripyrrane 157 was condensed with 2,5-diformylthiophene in the presence of TFA followed by oxidation with 0.1 aqueous FeCl₃ solution of yielded the thia azuliporphyrin 154 in 45% yield (Scheme 28). Similarly, the condensation of tripyrrane 157 with 2,5-diformylthiophene did not give the expected oxathialiporphyrin 156 but gave a mixture of three fully aromatic oxacarbaporphyrins 158a−c in a combined yield of 15% (Scheme 28). The compounds 158a−c were formed due to ring contraction of the seven-membered ring as observed previously for related aza analogues[133].

The free base forms of thia- and selenazuliporphyrins 155 exhibited borderliner aromatic properties that was enhanced on protonation as confirmed by detailed UV−visible and NMR studies. The azuliporphyrins were susceptible to nucleophilic attack to give carbaporphyrin adducts because of the electron deficient cycloheptatriene ring[133]. The thia- and selenazuliporphyrins 154 and 155 also showed similar reactivity[132]. On addition of pyrrolidine to 154 and 155 they gave the corresponding pyrrolidine adducts 159 and 160, respectively (Scheme 29). However, the hetero azuliporphyrins 154 and 155 requires more pyrrolidine as compared to the aza analogue to form pyrrolidine adducts. This was attributed to the larger size of sulfur and selenium atoms, which reduces the favorability of pyrrolidine adducts by decreasing the planarity of the macrocyclic core. The reactivity of 154 and 155 was further explored with alkaline solutions of tert-butyl hydroperoxide[132]. 154 was treated with t-ButOOH in the presence of t-ButOK, an inseparable mixture of 161a in 10% yield. However, when 154 was treated with t-ButOOH in the presence of t-ButOK, an inseparable mixture of 161a and 161b was formed in 50% yield (Scheme 29).

Similarly, 155 on treatment with tert-ButOCl gave 162a in 10% yield and when treated with KOH gave two major products 162a and 162b, which were separated by flash column chromatography. The tripyrrane 157 was condensed with 2,5-diformylthiophene in the presence of TFA followed by oxidation with 0.1 aqueous FeCl₃ solution of yielded the thia azuliporphyrin 154 in 45% yield (Scheme 28). Similarly, the condensation of tripyrrane 157 with 2,5-diformylthiophene did not give the expected oxathialiporphyrin 156 but gave a mixture of three fully aromatic oxacarbaporphyrins 158a−c in a combined yield of 15% (Scheme 28). The compounds 158a−c were formed due to ring contraction of the seven-membered ring as observed previously for related aza analogues[133].

The UV−visible and NMR studies of the carbaporphyrins 161 and 162 clearly showed that these hetero carbaporphyrins like aza carbaporphyrins are completely aromatic.

Chandrashekar and co-workers[134] also synthesized the thia[163] and selenazuliporphyrins[164] by following the “3+1” strategy used by Lash[130] to synthesize several aza carbaporphyrins. The thia- and selenazuliporphyrins 163 and 164 were prepared by acid catalyzed condensation of 33 and 34, respectively, with azulenyl-1,3-dicarboxaldehyde in dichloromethane followed by DDQ oxidation[134] (Scheme 30). They also observed borderline aromaticity for these hetero azuliporphyrins in free base form and enhanced aromatic behaviour in their protonated form using absorption and NMR studies.

The X-ray structure solved for 163 indicated that the molecule was completely planar and azuline moiety was in the plane defined by four meso-carbon atoms[134] (Fig. 20). The aromatic nature was evident from the smaller C−π−mesity of 163 and C−π−mesity of 164 with azulene-1,3-electric dipole distance of 2.53(1) Å, bond angle 177.00(18)° interaction present inside the azuliporphyrin cavity. The interesting aspect of the structure was the observation of non-classical hydrogen bonding interactions, such as C−H−π interactions between one of the β-hydrogen atoms of the pyrrole ring and the π-cloud of the meso-mesityl ring [C−H distance 0.950(2) Å, H···π distance 2.79(1) Å, C−H···π angle 137.10(12)°]. These C−H···π interactions helped in the formation of a one dimensional zigzag polymeric supramolecular array where the two adjacent porphyrin rings were aligned perpendicular to each other [134].

Although Lash and co-workers reported rich coordination chemistry for aza azuliporphyrins[123,126] and showed that the azuliporphyrins form very interesting organometallic derivatives with various metals, such as Ni(II), Pd(II), Pt(II) and Ag(II),
there have been no reports on metallation studies of hetero analogues of azuliporphyrins.

Chandrashekar and co-workers also synthesized the hetero analogues of benziporphyrins \[135\] by following Lash’s synthetic strategy of carbaporphyrins \[130\]. The oxa and thia derivatives of oxybenziporphyrins 165 and 166 were synthesized by “3 + 1” acid catalyzed condensation of 5-formyl salicylaldehyde with corresponding modified tripyrranes 32 and 33, respectively (Scheme 30). In \(^1\)H NMR, the upfield shifts of the inner CH and NH protons of 165 (−3.5 and −4.7 ppm) and 166 (−4.32 and −2.90 ppm) supported the aromatic nature of the macrocycles. The absorption spectra of 165 and 166 showed strong Soret type bands in 430–480 region and multiple Q-bands in the 500–750 region because of the porphyrinoid nature of the compounds. These observations were in line with the earlier observations made on aza carbaporphyrins. The aza oxybenziporphyrin forms an organometallic complex with Pd(II) \[6\]. Chandrashekar and co-workers also successfully synthesized an organometallic palladium derivative of 165 and the spectroscopic data indicated the retention of aromatic character of porphyrin on metal insertion \[135\].

Lash and co-workers by following their well established strategy synthesized a series of \(\beta\)-substituted and meso-unsubstituted S and O containing oxybenziporphyrins 167, 168, oxopyriporphyrins 169, 170 and benzocarbaporphyrins 171, 172 \[136,137\] by condensing the appropriate modified \(\beta\)-substituted tripyrranes 173 and 174 with 5-formyl salicylaldehyde, 3-hydroxy-2,6-pyridinedicarboxaldehyde and indene-1,3-dicarboxaldehyde in dichloromethane in the presence of trifluoroacetic acid followed by oxidation with DDQ (Scheme 31). UV–visible spectra of all hetero carbaporphyrins showed strong Soret bands and their \(^1\)H NMR exhibited large diatropic ring currents similar to their corresponding aza analogues, supported their aromatic nature. This kind of carbaporphyrin was known to form novel organometallic complexes. The organometallic Ni(II), Pd(II) and Pt(II) complexes of 171 were prepared and the studies indicated that all three complexes retained their aromatic character \[136,137\]. The X-ray structure solved for Pd(II) complex of 171 \[137\] exhibited a planar macrocycle with dihedral angles of the component pyrrole, furan and indene rings all \(\leq 2.1^\circ\) relative to mean \[18\] annulene plane were (Fig. 21).

Recently, Miyake and Lash reported the synthesis of a new class of heteroatom substituted benziporphyrins \[138\] using a
Scheme 31. Synthesis of hetero analogues of oxybenzi, oxypyri and benzocarbaporphyrins.

Scheme 32. Synthesis of hetero benzoporphyrins.

Scheme 33. Synthesis of tetrabenzoporphyrins.
The 7a or 7b were treated with 1.2 equivalents of OsO₄ in CHCl₃/pyridine for 24 h followed by quenching with H₂S and column chromatographic purification gave chlorin 192 as a major product (20%) and an isomeric mixture of two bacteriochlorins 193 as minor products (<5%) (Scheme 34). ¹H NMR spectroscopy confirmed that OsO₄ only reacts with double bonds of the pyrrole(s) to yield 192 and 193 when treated with an aqueous solution of KMnO₄ in the presence of 18-crown-6, underwent oxidative ring opening reaction and formed the dithiaporpholactone 194.

The UV–visible spectra of 192 showed a broadened Soret band and the longest wavelength absorption band (λ_max = 687 nm) was only minimally more intense and surprisingly little blue shifted when compared to the porphyrin 7 (λ_max = 699 nm). The UV–visible spectra of both the isomers of 193 were identical and showed the typical three band pattern of the bacteriochlorin chromophore. The absorption bands of 193 were significantly red shifted (λ_max = 734 nm) when compared to the porphyrin 7 [140].

9.5. Heteroatom substituted confused porphyrins

N-confused porphyrins, a group of porphyrin isomers that have an inverted pyrrole sub-unit were independently isolated and characterized by Furuta et al. in Japan [141] and Latos-Grażyński and co-workers in Poland [142] in 1994. Since N-confused porphyrins have the presence of inner CH, external and internal nitrogen atoms, these porphyrins exhibited very interesting metal coordination properties, such as being organometallic in nature, exhibiting multivalency and formation of inner and outer coordination complexes and supramolecular structures [143–153]. Thus, the N-confused porphyrins have been explored to synthesize metal complexes in various oxidation states, such as Ni(II), Pd(II), Ag(III), Sb(V), Cu(II), Fe(II), Rh(I) and Zn(II) [154]. Furthermore, Furuta et al. recently synthesized unique N-fused porphyrins [155,156] and cis-doubly N-confused porphyrins [157–159] and studied their metal bonding properties [160]. Recently, some confused heteroporphyrins have appeared. In heteroporphyrins, the confusion can occur with the pyrrole ring or with the other heterocycle, such as thiophene, furan, selenophene and tellurophene of porphyrin macrocycle. Thus, these porphyrins were sub-classified into N-confused heteroporphyrins and heteroatom confused heteroporphyrins.

9.5.1. N-confused heteroporphyrins

Lee and Kim [161–163] synthesized the first N-confused 21-thiaporphyrin 195 and 21-oxaporphyrin 196 by 3 + 1 condensation of 2,4-bis(α-hydroxy-α-phenylmethyl)pyrrole or its N-alkyl derivative 197 with modified tripyrrane 33 and 32 respectively under mild acidic conditions (Scheme 35). In 195 and 196, the confused pyrrole was in the position trans to the thiophene and furan rings, respectively. Chandrashekar and co-workers [164] synthesized, by using different precursors, the N-confused 21-selenaporphyrin 198 in addition to the 195 and 196 having a
confused pyrrole opposite to the heteroatoms. The tripyrrane containing the middle N-confused pyrrole ring 199 was condensed with the corresponding diol 21, 20 and 22 under standard conditions and afforded 195, 196 and 198, respectively, in 19–32% yields (Scheme 36a). The advantage of Chandrashekar and co-workers strategy of using 199 as a synthon resulted in the exclusive formation of the desired N-confused heteroporphyrins in high yields with only a trace amount of normal porphyrin making their column separation very easy.

Latos-Grażyński and co-workers [165] synthesized N-confused 21-selenaporphyrin 200 in which the confused pyrrole ring was adjacent to the selenophene ring unlike 198 in which the confused pyrrole was opposite to the selenophene ring. The compound 200 was obtained as a side product in 1% yield along with the expected 21-selenaporphyrin 4 in 19% yield in a typical acid catalyzed condensation of 22 with 24 (Scheme 36b). Similarly they [166] also obtained the N-confused 21,23-dithiaporphyrin 201 as one of the products in 4.7% yield by acid catalyzed condensation of 21 with pyrrole (Scheme 36c).

A detailed NMR studies has been carried out on free base and protonated forms of N-confused heteroporphyrins at different temperatures to identify the tautomers. Lee et al. [162] proposed the existence of three different tautomeric forms of N-confused porphyrins 195a and 196a depending on the location of the inner NH proton. (Chart 14). In tautomers I and II, the hydrogen was located on either of the inner pyrrole nitrogen atoms whereas in tautomer III, the proton was located on the nitrogen of the N-confused ring. The tautomer I was the only stable form for 21-oxaporphyrin 196a. However, studies on 21-thiaporphyrin 195a suggested that tautomer III was the major and tautomer I was the minor isomer at room temperature. Furthermore, studies at 223 K suggested that 195a existed in all three tautomeric forms I, II and III in the ratio 1:0.5:1. Interestingly, the N-alkyl substituted N-confused porphyrins existed only as tautomer III because of the bulkiness of the alkyl group [163]. Density functional theory also supported the existence of different tautomeric forms for N-confused 21-thiaporphyrins [167].
Detailed NMR studies were carried out by Chandrashekar and co-workers for N-confused porphyrins \textsuperscript{195a, 196a and 198} [164]. They also observed a single dominant tautomer as in I for 196a. Furthermore, their studies also confirmed the existence of three different tautomeric forms in equilibrium for 195a at low temperature. However, they claimed that for 195a, the tautomer I was the major component rather than tautomer III at room temperature based on NMR and X-ray structural studies [164]. In \textsuperscript{1}H NMR, the observation of the inner NH signal in the shielded region and the outer NH signal in the deshielded region on careful titration of 195a with TFA supported the tautomer form I was the dominant at room temperature. The X-ray structure shows formation of a cyclophane dimer in the unit cell because of the presence of strong hydrogen bonding interaction between the inner NH of one molecule and the outer nitrogen of the other molecule; this may support the view that the predominant form of 195a at room temperature is tautomer I.

Latos-Grażyński and co-workers [165] also proposed the existence of the three tautomers IV, V and VI for N-confused 21-selenaporphyrin 200 in which the N-confused pyrrole was adjacent to the selenophene ring (Chart 15). NMR studies on 200 indicated that in pyridine-\textsubscript{d5}, only tautomer VI was exclusively formed but in chloroform-\textsubscript{d}, the tautomers V and VI were formed in equilibrium.

The N-confused heteroporphyrins exhibited split Soret bands in the region 425–450 nm and Q bands in the region 500–750 nm [162–166]. The presence of split Soret bands indicated the less planar character of N-confused heteroporphyrins relative to regular heteroporphyrins. The crystal structures of N-confused heteroporphyrins 195a [164] and 200 [165] have been solved. The structure of 195a shown in the Fig. 22 clearly indicated the non-planarity of the macrocycle in a ruffled conformation where the meso-carbons were formed alternately above and below the mean plane defined by four meso-carbon atoms. The dihedral angles were 2.82(6)° for the thiophene ring, 21.11(9)° and 31.23(9)° for the two pyrrole rings, respectively, indicating that the N-confused pyrrole ring showed the maximum deviation [164]. The presence of the large sulfur atom increased the repulsion between the inner NH and the sulfur atom resulting in the deviation of the pyrrole away from the mean plane. The
alteration of π-delocalization in 195a was evident in the significant changes in Cα–X, Cα–Cβ and Cβ–Cβ distances relative to free thiophene and pyrrole units. The packing diagram of 195a showed that the unit cell contained two molecules which were linked to each other through a non-covalent weak N−H···N and C−H···N intermolecular hydrogen bonds involving the pyrrole NH and N atom of the N-confused ring and C atom of pyrrole ring. These interactions lead to a cyclophane-like dimeric structure where the two N-confused rings were almost one above the other [164]. In addition, there were two intramolecular N−H···S hydrogen bonds and one C−H···S hydrogen bond in each molecule between N1–H, N3–H, pyrrole C13 and thiophene sulfur with an average distance of 2.74 and 3.45 Å for N−H···S and C−H···S hydrogen bonds, respectively. The X-ray structure of 200 (Fig. 23) exhibited saddle distortion [165]. The Se–Cα, Cα–Cβ and Cβ–Cβ distances of 200 were similar

Fig. 22. X-ray structure of 195a. (a) Top view and (b) side view (reproduced with permission from Ref. [164]).
to those of 4 indicating the perseverance of aromatic character of the macrocycle, on inversion of one of the pyrrole ring in 200.

9.5.2. Heteroatom confused heteroporphyrins

Latos-Grażyński and co-workers [168,169] prepared the first S-confused porphyrin 202 by condensing 2,4-bis(phenylhydroxymethyl) thiophene 203 with benzaldehyde and pyrrole via one pot two step reaction or by the [3+1] condensation of the 203 and 5,10-diphenyltripyrrane 24 (Scheme 37). The oxidation of 202 with DDQ or with an excess of p-chloranil gave a new compound 204. The ^1H NMR study on 202 showed that the inner NH appeared as a singlet at 5.81 ppm and inner CH resonance of the inverted thiophene ring appeared at 4.76 ppm suggesting that this porphyrinoid exhibiting borderline aromaticity. However, an ^1H NMR study of 204 exhibited typical aromatic features with inner CH and two inner NH resonances appearing at −5.31, −3.37 and −2.93 ppm, respectively [168].

Pawlicki and Latos-Grażyński [170] attempted to synthesize the O-confused oxaporphyrin 205 by condensing 2,4-bis(phenylhydroxy methyl)furan 206 with p-tolylaldehyde and pyrrole in a 1:2:3 molar ratio under mild acid conditions (Scheme 38). However, this condensation did not yield the expected O-confused oxaporphyrin 205 but gave the pyrrole addition product 207 in 10% yield. The electronic absorption spectrum of 207 showed a strong Soret band and a set of four Q-bands like any other aromatic carbaporphyrinoids [170]. The aromatic nature and the ring current effects of the compound 207 were also evident in the upfield positions of the inner CH (δ = −5.11 ppm) and inner NH protons (δ = −2.4, −2.79 ppm). The macrocycle 207 can act as a dianionic or trianionic ligand and complexes metal ions to match the oxidation state of
Scheme 38. Synthesis of pyrrole appended O-confused porphyrins.

metal ion. Thus, the Ni(II), Pd(II) and Ag(III) complexes of 207 were prepared under standard metallation conditions [170]. The insertion of Ni(II) and Pd(II) metal ions resulted in related dehy- drogenated organometallic complexes 207a and 207b, respectively, in which the metal ions were coordinated to three pyrrolic nitrogen atoms and the trigonally hybridized C21 atom of the inverted furan [170]. The electronic spectra of 207a and 207b showed several Soret like bands and less intense Q bands with low extinction coefficients compared with 207 indicating that the aromatic character of ligand 207 was lowered on metal complex- ation. Interestingly, the insertion of Ag(III) into 207 on treatment with silver acetate followed by addition of ethanol initially gave a stable Ag(III) complex 207c which was substituted at the C3 position by the ethoxy and pyrrole moieties. However, when this macrocycle 207c was treated with TFA it resulted in a new aromatic Ag(III) complex 207d due to elimination of the ethoxy group. The compound 207d was converted back to 207c on treat- ment with sodium ethoxide in ethanol [170].

A set of canonical structures VII, VIII and IX was pro- posed for 207a, 207b, 207d (Chart 16) to account for their non-aromatic and aromatic behavior [170]. The canonical struc- ture VII was non-aromatic with less interaction between the macrocycle and appended pyrrole moiety. However, the struc- tures VIII and IX were aromatic and the direct conjugation between the appended pyrrole fragment and the carbaporphyrinoid π-system was expected for VIII and IX structures. The electronic structures of 207a, 207b, 207d (Chart 16) were a com- bination of aromatic and non-aromatic canonical structures and the most aromatic character observed for 207d was due to the dominant contribution of canonical structures VIII and IX and relatively less aromatic nature noted for 207a and 207b was due to the major contribution from canonical structure VII. Support

Table 6

<table>
<thead>
<tr>
<th>Compound</th>
<th>Appended pyrrole protons (ppm)</th>
<th></th>
<th></th>
<th>NH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrrole</td>
<td>6.22 6.22 6.68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>207</td>
<td>5.54 5.82 6.33 7.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>207a</td>
<td>6.34 6.17 6.76 8.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>207b</td>
<td>6.36 6.20 6.79 8.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>207d</td>
<td>6.60 6.40 7.27 9.81</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

for the contribution of different canonical structures for metal complexes on 207 was clearly evident from $^1$H as well as $^{13}$C NMR chemical shift values of the appended pyrrole moiety. The $^1$H NMR chemical shifts of the appended pyrrole moiety of 207 and its metal complexes shown in Table 6 indicated that there was a gradual increase in the chemical shift values of appended pyrrole moiety in the series 207, 207a, 207b, and 207d. The largest shift value observed for 207d was due to the effective conjugation between the macrocycle and the appended pyrrole moiety [170].

The structures of 207a and 207c were determined by X-ray crystallography [170]. In 207a, the macrocycle was only slightly distorted from planarity (Fig. 24) and the dihedral angle between the macrocycle and the appended pyrrole planes reflects the biphenyl-like arrangement with the NH group pointing out towards the adjacent phenyl ring on the C5 position. The Ni–N distances in 207a were comparable to those of other diamagnetic Ni(II) porphyrins and Ni–N bond length was similar to other Ni(II) carbaporphyrinoids where the trigonal carbon atom coordinated to the metal ions. The C9–C9 and C9–C9 bond lengths were changed in 207a compared to free furan indicating that π-delocalization through the furan ring was altered. The bond length changes in the furan ring of 207a were in between the range of furan ring which was built into non-aromatic and aromatic macrocycles and supporting the view that the canonical structure VII is the dominant form for this macrocycle. The crystal structure solved for 207c [170] showed that it exhibited only slight distortion from planarity (Fig. 25).
Fig. 25. X-ray structure of \(207c\). (a) Top view and (b) side view (reproduced with permission from Ref. [170]).

Ag–C distances in \(207c\) were comparable to those in other silver(III) carbaporphyrinoids [124].

10. Unusual reactivity of telluraporphyrins

The telluraporphyrins although not very well studied, possess unusual properties and reactivity compared to their lighter chalcogen analogues. Latos-Grażyński et al. [171] first noted the unusual reactivity of 21-telluraporphyrin \(5\) by treating it with \(m\)-chloroperoxybenzoic acid. When \(5\) was treated with excess \(m\)-chloroperoxybenzoic acid, \(2\) was formed in good yield. However, when \(5\) was treated with a limited quantity of oxidant, first the green intermediate species \(208\) was formed, which on further treatment of additional oxidant gave \(2\). The two compounds

208 and 2 were also formed when 5 was exposed to air [171]. The exposure of 5 to air for few minutes gave 208, which on prolonged exposure to air converted to 2 (Scheme 39). 208 can be reduced back to 5 by treating it with either zinc-amalgam or sodium dithionate [171]. The 208 was isolated and characterized by X-ray diffraction analysis. The structure of 208 [171] indicated that it was forming a zwitterions by transferring the hydrogen atom of the trans pyrrole nitrogen to the oxygen atom with a hydroxyl group attached to the tellurium atom (Fig. 26). The hydroxyl group attached to the tellurium atom interacted with trans pyrrole ring via a weak hydrogen bond resulting in bending the trans pyrrole ring upward towards the hydroxyl group.

Recently, Detty and co-workers [172] solved the crystal structure of 5c and isolated the tautomeric form of 21-telluraporphyrin in which the H-atom resides on a pyrrole N that was cis to the tellurophene ring. The structure of 5c was only slightly distorted from planarity as noted previously for the other 21-telluraporphyrin 5b in which pyrrole ring bearing H-atom was trans to the tellurophene ring (Fig. 27). They also noticed that in 5c, the Te atom interacted with the H-atom of N3 through hydrogen bonding with a Te1 · · · HN3 distance of 1.827 Å. The Te atom also interacted strongly with N1 on the second cis pyrrole ring with a Te1 · · · N1 distance of 2.558 Å. The Te1 · · · N2 distance (3.173 Å) was nearly identical to that of 5b [172].

The reactivity of 5c was further explored by first oxidizing the 5c with air or chemically to 208 which was then treated with HCl for several seconds and afforded 209 (Scheme 40) [172]. The X-ray structure of 209 (Fig. 28) indicated that the porphyrin macrocycle was non-planar unlike the planar structure observed for 5c [172]. In 209, the Te atom was in the +4 oxidation state with two Cl atoms attached in the axial positions to Te in the center of a trigonal bipyramid (Fig. 28). The Cl–Te–Cl bond angle of 168.65° reflected the stereochemically active lone pair of electrons on Te1 in the equatorial plane of the trigonal bipyramid. The Te–Cl bonds are not equal in length, with the Te–Cl2 bond (2.58 Å) more elongated than Te–Cl1 bond (2.49 Å). The tellurophene ring was distorted from planarity with Te1 displaced from the plane of the four carbon atoms by 0.281 Å towards the
The high reactivity of 21-telluraporphyrins was further utilized recently by Latos-Grażyński and co-workers to synthesize a novel molecule 21-vacataporphyrin 210 [175]. The 210 was a hybrid of annulene and porphyrin and has a vacant space instead of a heteroatom bridge. 210 was synthesized in 55% yield by reacting 5b with HCl at refluxing temperature (Scheme 41). The 21-vacataporphyrin 210 was nearly planar as confirmed by X-ray analysis (Fig. 29) and possessed similar spectroscopic properties to that of porphyrin 1. The 210 has three nitrogen atoms and CH groups favorably prearranged for coordination to a metal ion although the metal coordination properties have not yet been reported.

Latos-Grażyński and co-workers [176] synthesized 21,23-ditelluraporphyrin with a flipped tellurophene ring 211 in 11% yield by following standard synthetic methodology used for 21,23-diheteroporphyrins (Scheme 42). The 211 was the first example of the inverted structure of the 18-π-electron porphyrin-like frame with four five-membered rings linked by four methane carbon atoms. The X-ray structure solved for 211 (Fig. 30) was attributed to the size of the tellurium atoms [176]. One of the tellurophene moieties (Te23) was coplanar with the two adjacent pyrrole rings while the second tellurophene ring (Te21) was directed away from the center of the macrocycle (Fig. 30). The degree of distortion was reflected by a dihedral angle between the plane of the meso-carbon atoms and the tellurophene plane of 123.0(2)°. The electronic spectrum of 211 did not show a strong Soret band but showed three major bands of comparable intensities at 348, 464 and 668 nm. However, the protonated form 211 showed the presence of Soret like band at 490 nm and a less intense band at 767 nm, which was attributed to the more aromatic nature of the protonated form compared with the neutral species.

In 1H NMR, the tellurophene protons at δ 8.53 and 6.08 ppm, respectively, were due to the regular and flipped tellurophene rings [176]. However, protonation with TFA resulted in a regular structure in which Te21 and Te23 tellurophene atoms were simultaneously directed towards the center of the macrocycle (X-HH2, Chart 17). This was evident in 1H NMR, which showed only one signal at δ 8.03 corresponding to the tellurophene ring protons. Also the NH resonances appeared in high field region (~0.7 ppm) due to the changed ring current effect supported the regular structure [176]. Furthermore, based on the NMR studies at different temperatures, the molecule 211 appears to interchange between two energetically and structurally identical flipped forms XI and XII (Chart 17).
11. Water-soluble heteroporphyrins

Water-soluble porphyrins are important materials with significant applications in many applied fields including biology and medicine [177]. Specifically, the water-soluble porphyrins are potential photo sensitizers for photodynamic therapy (PDT) of cancer in which light and endogenous oxygen, facilitated by a photo sensitizer, on irradiation produces a cascade of biochemical events that inactivate cancer cells [177]. Water-soluble porphyrins with an N4 core, such as 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin (TPPS) have been studied extensively as sensitizers for PDT and have shown promising results. However, the N4 water-soluble porphyrins besides exhibiting neurotoxicity, also absorbs weakly near the 630 nm region where light has greater penetration into the tissue. The presently available porphyrin PDT drug, Photofrin, also absorbs weakly in the same region and hence is not an ideal drug [177]. Thus, the water-soluble heteroatom substituted porphyrins, which absorbs in longer wavelength region (650–700 nm) can be explored as photo sensitizers for PDT.
Chandrashekar and co-workers [178,179] synthesized the first anionic water-soluble tetrasulfonated 21-thiaporphyrin 212 and 21,23-dithiaporphyrin 213 by sulfonation of porphyrins with chlorosulfonic acid under mild reaction conditions. Comparison of the spectroscopic and electrochemical properties of 212 and 213 with regular anionic water-soluble porphyrins showed the expected bathochromic shifts of the absorption bands, and red shifts of the fluorescence bands with reduced quantum yields. Oxidation and reduction were harder and easier, respectively. The Cu(II) and Ni(II) derivatives of 212 were prepared and the electrochemical studies indicated the reduction of the metal center. The aggregation properties of 212 and 213 were similar to regular anionic water-soluble porphyrins [179]. Latos-Grażyński and co-workers [180,181] have used similar reaction conditions and prepared the disulfonated water-soluble
21-selenaporphyrin in which the sulfonated groups were at \( \alpha \)-position (the structure is not shown in Chart 18).

Detty and co-workers [182, 183] recently synthesized the tetratosulfonated water-soluble 21-thiaporphyrin 212, 21,23-dithiaporphyrin 213 and 21,23-diselenaporphyrin 214 as tetrasodium salts by sulfonation of the corresponding porphyrin by treatment with sulfuric acid followed by treatment with NaOH. They have also synthesized a series of disulfonated derivatives of heteroporphyrins 215–218 under similar reaction conditions.

Detty and co-workers further synthesized a series of water-soluble heteroporphyrins bearing 1–4 carboxylic acid groups 219–223 by saponification of the corresponding esters [184]. The sulfonated and carboxylated heteroporphyrins were evaluated in vitro as photo sensitizers for photodynamic therapy and some showed promising results.

We synthesized [57, 60] a series of the first cationic water-soluble 21-thiaporphyrins (224a–c and 226a–c) and 21-oxaporphyrins (225a–c and 227a–b) containing two and three
N-methylypyridinium ions at *meso*-positions by methylation of the *meso*-pyridyl porphyrins with 500-fold excess of CH3I in CH2Cl2 at refluxing temperature overnight (Chart 19). The absorption and fluorescence bands of these cationic water-soluble heteroporphyrins as expected were red shifted compared to tetraakis-N-methylpyridinium/porphyrin because of the presence of the heteroatom in the core [60]. However, these compounds have not been tested for any applications.

12. Conclusions

The present review reflects that even though the mono- and diheteroporphyrins have been known for almost three and half decades, there have been significant developments in synthetic heteroporphyrin chemistry over the past 5–6 years. Up until 1998, very few new heteroporphyrin derivatives were known and most of the research till then was focused on syntheses and structures of metal complexes of simple to make heteroporphyrin ligands and stabilization of metals in unusual oxidation states. In the last few years, heteroporphyrin chemistry has advanced rapidly and almost every hetero analogue(s) of porphyrins and their derivatives, such as chlorins, corroles, car- baporphyrins, confused porphyrins, and other porphyrins and diheteroporphyrins have been synthesized and studied for their potential use for various applications as a substitute for regular porphyrins. The most important synthetic developments in heteroporphyrin chemistry during the 1999–2005 period are: (1) new and modified synthetic routes to prepare heteroporphyrins, (2) first metal complex of 21,23-dithiaporphyrin, (3) *meso*-unsubstituted porphyrins and their functionalization and *meso*-substituted porphyrins having thienyl, furyl and sterically crowded dendrons, (6) chlorins and bacteri- ochlorins, tetraheaporphyrins, (7) carbaporphyrins and their organometallic complexes, (8) N-confused as well as heteroatom-confused porphyrins, (9) corroles and their metal complexes and (10) water-soluble porphyrins. Thus, these novel heteroanalogues of porphyrins set the stage for further research for new methods and new heteroporphyrin systems. In terms of future efforts, we expect the synthesis of many other heteroporphyrins with cores having various heteroatom combinations and also large complex systems, such as a porphyrin arrays containing four or more different porphyrin cores connected via covalently or non-covalently, to be studied for their potential applications in molecular electronics and other related applied fields.

More synthetic heteroporphyrin chemistry will be carried out in the coming years to develop all the possibilities of this fascinating family of molecules.

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