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Heptaphyrins: Expanded porphyrins with seven heterocyclic rings[¶]

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Abstract. Expanded porphyrins containing seven pyrrole/heterocyclic rings linked in a cyclic fashion are termed heptaphyrins. The number of *p*-electrons in heptaphyrins depends on the number of *meso* carbon bridges used to link the heterocyclic rings, accordingly heptaphyrins with 28*p*-electrons and 30 *p*-electrons are reported to date. Both condensation reactions of the appropriate precursors and acid-catalysed oxidative coupling reactions have been utilized to synthesise the heptaphyrins. The 30*p* heptaphyrins exhibit rich structural diversity where some of the heterocyclic rings in the macrocycle undergo a 180° ring flipping. An overview of the synthetic methods employed for the synthesis of heptaphyrins, their spectroscopic properties, structural behaviour and aromatic properties are highlighted in this paper.

Keywords. Heptaphyrins; expanded porphyrins; core modification; aromaticity; ring inversion.

1. Introduction

The syntheses of expanded porphyrins continue to attract the attention of chemists because of their diverse biological applications such as: anion receptors, photosensitizing agents, MRI contrast agents[1] etc. They are also of interest, theoretically, to study the fundamental property of aromaticity in systems containing more than 18*p*-electrons.[2] This has led to syntheses of various expanded porphyrins such as 22*p* sapphyrins,[3] 26*p*

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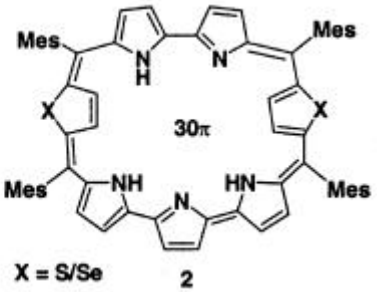

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[¶]Dedicated to Professor C N R Rao on his 70th birthday
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rubyrins,[4] 28π and 30π heptaphyrins,[5] 32π, 34π, 36π, 38π octaphyrins,[5a,6] 40π turcasarin,[7] 48π dodecaphyrins, 64π hexadecaphyrin,[8] 80π icosaphyrin and 96π tetracosaphyrin.[9] Of these the 22π sapphyrin and 26π rubyrins are well studied with respect to their structural behaviour,[3c,4c,10] anion receptor properties,[4c,11] metal coordination[12] and aromaticity. Even though the syntheses of expanded porphyrins containing more than 26π electrons have been achieved, the detailed studies on their structural behaviour, coordination properties and aromaticity are not well understood and attempts are on the way to exploit these properties for further applications. For example, the octaphyrins and the higher order systems exhibit non-planar conformation thus losing aromaticity.

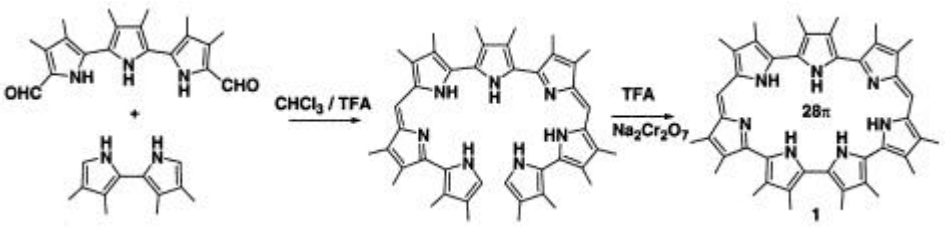
Very recently Sessler and co-workers[13] and Chandrashekar and co-workers,[14] have succeeded in synthesizing expanded porphyrins containing more than 26π-electrons and have shown that aromaticity in these systems is sustained because of their planar structure. Specifically it has been shown that the expanded porphyrins containing seven heterocyclic rings linked in a cyclic fashion exhibit aromaticity depending upon the nature of the link and the number of *meso* carbons used to bridge the heterocyclic rings. For example, heptaphyrin, **1**, which has only two *meso* carbons with 28π-electrons is shown to be non-aromatic,[5a] while the heptaphyrin, **2**, which contains 30π-electrons is *aromatic*.[5b] In this paper an attempt has been made to give an overview of all methodologies used for their syntheses, structural behaviour, anion complexation and aromatic behaviour of heptaphyrins containing seven pyrrole/heterocyclic rings.

2. Results and discussion

2.1 *Heptaphyrins with two meso carbons*

Sessler and co-workers[5a] reported the first heptaphyrin, **1**, which was found to be non-aromatic in nature. The seven pyrrolic unit was synthesised in two steps; a condensation of two bipyrrolic units with terpyrrole dialdehyde was followed by an oxidative coupling of linear heptapyrrolic oligomer under acidic conditions (scheme 1). Presence of only two *meso* carbon bridges in the macrocycle led to the increased pyrrole–pyrrole direct bonds.

The decrease in the number of *meso* carbons reduced the number of π-electrons from the expected 30π to 28π and hence was non-aromatic in nature. In the electronic absorption spectrum, the freebase displays a broad band at 507 nm and for the protonated form a band at 613 nm is observed. The ε values for these absorptions are of the order 10^3, indicating the non-porphyrinoid/aromatic characteristics for the macrocycle. Characterisation by ^{1}H NMR spectroscopy for the diprotonated form exhibited four NH signals, in the ratio 2:2:2:1, in the low field region from 15·9 to 18·2 ppm indicating the non-aromatic character for the macrocycle. Its ability to bind anions is displayed by single



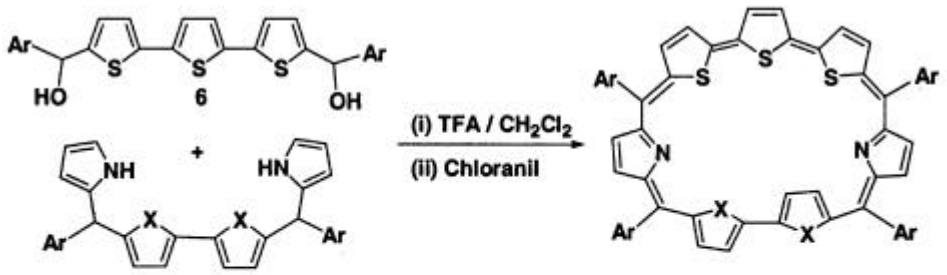
Scheme 1.

crystal X-ray diffraction of diprotonated adduct of sulphate. The macrocycle has a fairly planar structure, with all the NH's involved in the binding of the sulphate anion in the core of the macrocycle through N–H---O hydrogen bonding interactions.

2.2 *Heptaphyrin with four meso carbons*

Based on this result, we set out to work on systems having heterocyclic rings which could maintain aromatic features as observed in the case of sapphyrins[3] and rubyrins.[4] Theoretically, insertion of an extra heterocyclic ring in a rubyrin should yield the desired 30π aromatic heptaphyrin. Rubyrins are synthesised either through condensation or coupling of appropriate precursors. Therefore adding an extra heterocyclic ring in one of the precursors should be the easiest route for accessing the 30πheptaphyrin. On the lines of a [4 + 2] condensation of modified tetrapyrranes and modified diols for rubyrins, we designed a [4 + 3] condensation with tetrapyrranes and terthiophene diol. An acid-catalysed condensation of dithia tetrapyrrane, **3a**, and terthiophene diol, **6** (scheme 2), and subsequent oxidation by chloranil yielded the desired aromatic 30πheptaphyrin, **7a** in 20% yield. Similar products, **8a** and **9a**, were obtained in 21 and 10% yields respectively by reacting terthiophene diol, **6**, with diselena, **4a**, and dioxa, **5a**, tetrapyrranes. Further a [5 + 2] condensation of pentapyrrane and modified diols also yielded the 30π heptaphyrins, **7b**–**9b**, in almost the same yield as in the case of [4 + 3] condensations. Also the change in the *meso* substituents did not affect in the nature or the yield of the product formed. The heptaphyrins, **7**–**9** contain 30πelectrons and are in accordance with ($4n$ + 2) Huckel's rule, which are expected to be aromatic.

The aromatic nature of the heptaphyrins, **7**–**9**, was proved by various analytical methods. The Soret-like absorption in the electronic spectra was strongly red-shifted, with respect to 26π rubyrins, both due to the increased number of π-electrons and the heteroatom substitution. They absorb in the region 555–575 nm, which on addition of acid is further red-shifted by 12–15 nm indicating the porphyrinoid like characteristics. The ε values are of the order of 10^5, which is higher by two orders of magnitude



	X	Ar
3a	S	Ph
3b	S	Mes
4a	Se	Ph
4b	Se	Mes
5a	O	Ph
5b	O	Mes

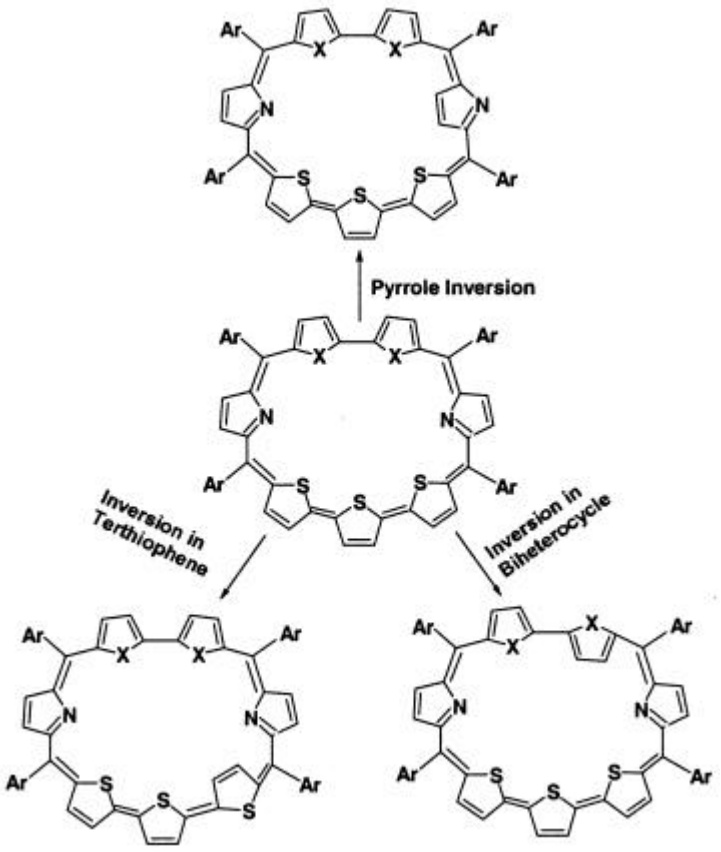
	X	Ar
7a	S	Ph
7b	S	Mes
8a	Se	Ph
8b	Se	Mes
9a	O	Ph
9b	O	Mes

Scheme 2.

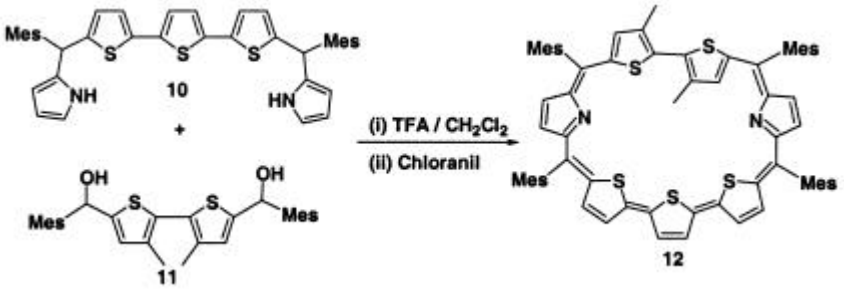
compared to the non-aromatic heptaphyrin, **1**. On protonation the ε values increase, signifying the aromatic and the porphyrinoid characteristics.

The proton NMR spectra for heptaphyrins, **7**–**9** reveal the unsymmetrical nature of the macrocycle. In the shielded region, in addition to the NH signals, two well-resolved doublets were observed at –5·22 and –5·39 ppm for **7b**. The ^{1}H–^{1}H COSY spectrum suggests correlation between these two signals. This observation suggests that one of the heterocyclic rings is inverted in the macrocycle and the ***b***-CH protons of the inverted macrocycle, which are experiencing the ring current are responsible for these signals. Such a ring inversion has been observed before for *meso* aryl sapphyrins[3c] and rubyrins.[4c] In order to find which of the heterocyclic rings is inverted, one can envisage three possibilities as shown in scheme 3.

They are: (a) One of the pyrrole rings could be inverted (b) One of the thiophene units in the bithiophene unit could be inverted (c) One of the thiophenes from the terthiophene unit could be inverted. The first possibility could be ruled out since; the NH signal for the protonated macrocycle is observed in the shielded region. This clearly indicates that the NH protons experience the ring current effect and this is possible only if the pyrrole rings are not inverted. On the other hand, ring inversions in the bithiophene or the terthiophene



Scheme 3.



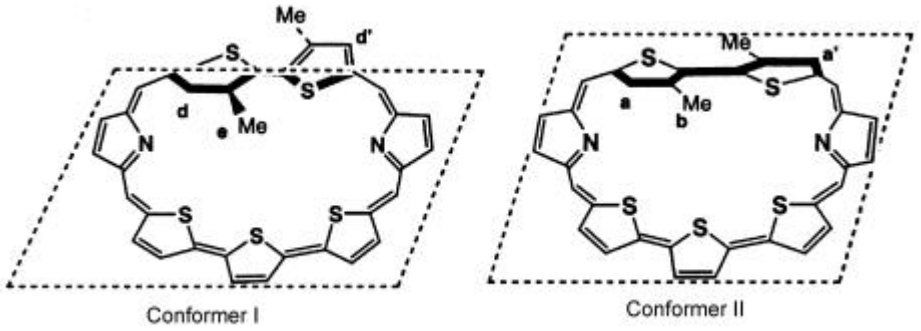
Scheme 4.

could be expected and it could not be confirmed by the above analysis. Also the symmetry of the molecule is almost the same irrespective of the ring inversion either in the bithiophene or in the terthiophene unit. A ^{77}Se NMR spectrum of the selena heptaphyrin, **8a**, recorded at room temperature exhibited two different signals at 557 and 537 ppm (with respect to dimethyl selenide) for the two selenium atoms revealing the difference in the magnetic environment for each selenium. This indicates the possible ring inversion in the biselenophene unit rather than in the terthiophene unit. To confirm this, an acid catalysed [5 + 2] condensation of the pentapyrrane, **10**, and *b*-substituted diol, **11**, was carried out to yield the desired *b*-substituted heptaphyrin, **12** (scheme 4) in 15% yield.

b-substituted thiophene was employed to differentiate between the two possibilities (b) and (c). In the case of ring inversion for the *b*-substituted rings, the *b*-substituent (methyl protons) will resonate in the shielded region, else two doublets from the thiophene unit of the terthiophene will be observed, thus giving the exact nature of the ring inversion. The similarity in the UV-Vis spectrum for both the *b*-substituted and unsubstituted heptaphyrins revealed identical structures for both the heptaphyrins. Further analysis through NMR spectroscopy confirmed the ring inversion in the bithiophene unit rather than in the terthiophene unit.

The *b*-substituted methyl groups on the two thiophene rings of the bithiophene unit resonated at different magnetic fields. Two signals for the methyl groups were observed at –3·26 and 2·7 ppm. Also, a singlet in the low field region at 9·25 ppm and a singlet in the up field region at –0·65 ppm were observed for the *b*-CH of the non-inverted and the inverted thiophene rings respectively. This is possible only when one of the *b*-substituted thiophene of the bithiophene unit is inverted. Even on protonation, these signals were observed except for slight deshielding/shielding proving the inverted state for the dication also. A careful analysis of the ^{1}H NMR spectrum showed the presence of two different conformers for the *b*-substituted heptaphyrin in the ratio 1 : 2.

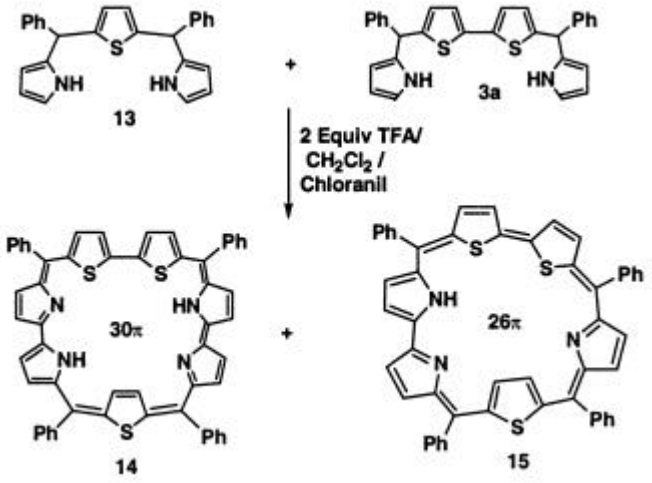
The possibility for two different conformers (conformer I and conformer II) could be visualized only based on the conformational positions for the *b*-substituted methyl groups. The close proximity between the two-methyl groups makes the bithiophene unit to be present in two different positions such that in one case both the thiophenes are non-planar to each other, while in the other case both the rings are co-planar with each other. A marginal difference in the chemical shift values for the methyl groups (–3·86 [e] and –4·34 ppm [b]) and *b*-CH protons of the inverted ring (–0·15 [d] and –0·64 ppm [a]) in the shielded region further supports such an assumption of the different conformations for



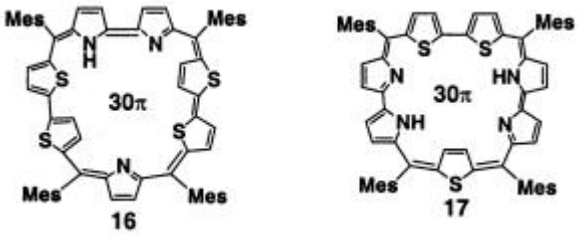
the bithiophene rings leading to two different conformations in the macrocycle. The ^{1}H NMR recorded at various temperatures did not show any signs of the two conformers leading to the formation of a single isomer. Also in the protonated form, the different conformations were retained as evidenced from the ^{1}H NMR spectrum.[5d]

After the successful synthesis of 30$p$heptaphyrins, attempts were made to synthesize other isomers of the heptaphyrins through a different approach. Oxidative coupling reactions[5a,13–15] have been exploited recently in the synthesis of expanded porphyrins. The relative ease and the requirement of simple precursors have made this methodology attractive enough for the synthesis of higher order expanded porphyrins. The syntheses of heptaphyrins and octaphyrins are classic examples for the success in this mode of synthesis. We also adopted this method to check for the formation of the heptaphyrins through easily available precursors. On the lines of [4 + 3] condensation, an [4 + 3] acid catalysed coupling of modified tetrapyrrane and tripyrrane was designed to check the feasibility for the formation of the heptaphyrins.

Coupling of dithia tetrapyrrane, **3a**, and thia tripyrrane, **13**, catalysed by TFA and subsequent oxidation by chloranil yielded the expected heptaphyrin, **14**, along with a novel isomer of rubyrin, **15** (scheme 5). Similar products were obtained with selenium derivatives also. This reaction was found to be dependent on the concentration of the acid employed, and tetrapyrrane was found to be reactive only at acid concentrations of 1·5 equivalents or above. At lower concentrations of acid, only rubyrin was isolated in higher yields. The formation of **15** is possible only due to the acidolysis of the tetrapyrrane and the tripyrrane under acidic conditions.[16] The fragments formed due to the acidolysis undergo recyclization to form the novel isomer of rubyrin, **15**. Whereas the formation of the heptaphyrin, **14**, is a straightforward coupling of the tetrapyrrane and the tripyrrane leading to the formation of two direct pyrrole-pyrrole bonds. These molecules also proved to be *aromatic* as analysed by various analytical methods. The UV-Vis spectrum for the heptaphyrins showed red shifts with respect 26$p$rubyrins, and further red shifts were observed upon protonation. The $e$values for heptaphyrin **14**, are of the order of 10^6, and are found to be an order higher in comparison to the heptaphyrins **7**–**9**. This is similar to the observation made for the heptaphyrins synthesised through condensation methods. The variation in the product formation was drastic when the bulkier mesityl group replaced the phenyl substituents on the *meso* carbons of the dithia tetrapyrrane. Subjecting the mesityl substituted precursors to oxidative coupling process as mentioned above, gave a new isomer of heptaphyrin **16** in addition to the expected molecule **17**.



Scheme 5.



The mesityl substituted dithia tetrapyrrane, **4b**, and the mesityl substituted thia tripyrrane under acidic conditions undergo cyclisation leading to the formation of heptaphyrin, **16**. The formation of the heptaphyrin can be attributed to the acidolysis of the tetrapyrrane, **4b**, alone. The fragments of the acidolysis recyclise to form the heptaphyrin having four thiophenes and three pyrrole rings. Even though acidolysis of dipyrromethanes and tripyrranes are known,[17] this is the first report of the acidolysis of the tetrapyrrane for the formation of expanded porphyrins.

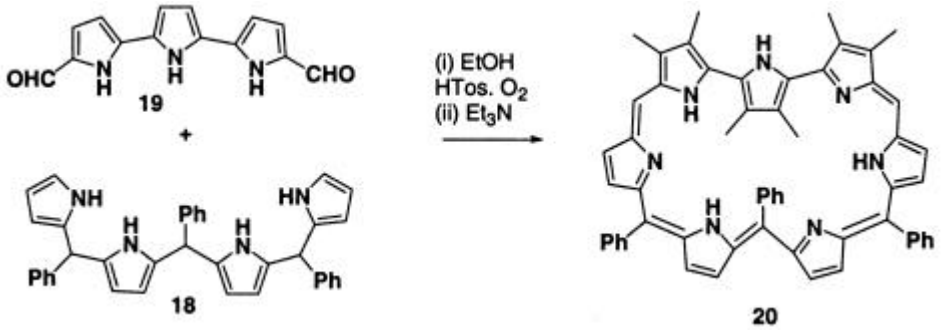
Table 1 lists the $\Delta\delta$ values (difference between the most shielded signal and the most deshielded signal in the ^{1}H NMR spectrum) observed for various heptaphyrins in both the freebase and protonated forms. The magnitude of these values has been used to assess the aromaticity in expanded porphyrins.[3c] The observed values here clearly suggest the aromatic nature of the heptaphyrins described in this work.

2.3 *Heptaphyrin with five meso carbons*

Very recently Sessler and co-workers[5c] were successful in synthesizing the all aza isomer of heptaphyrin having 30π-electrons in the conjugated pathway. In a similar approach as that of the [4 + 3] condensation, the tetrapyrrane with three *meso* carbons, **18**, was

Table 1. Δd value tabulated for heptaphyrins **7**, **8**, **9** and **16**.

	Freebase			Dication		
Heptaphyrin	$U_{(ppm)}$	$L_{(ppm)}$	Δd	$U_{(ppm)}$	$L_{(ppm)}$	Δd
7a	–2·03	10·87	**12·9**	–4·68	12·39	**17·17**
8a	–0·65	10·2	**10·85**	–4·52	12·22	**16·74**
9a	–1·69	10·98	**12·67**	–3·77	11·91	**15·68**
7b	–1·7	10·93	**12·63**	–7·08	12·97	**20·05**
8b	–1·66	10·2	**11·86**	–6·34	12·68	**19·02**
9b	–1·41	10·67	**12·53**	–5·77	12·53	**18·3**
16	–1·31	9·95	**11·26**	–5·65	10·89	**16·49**



Scheme 6.

condensed with tripyrrole dialdehyde, **19**, to obtain the heptaphyrin, **20**, with five *meso* positions (scheme 6) approximately in 15% yield.

The interesting feature of this heptaphyrin is the observation of different conformations in the solution state and the solid state. The NMR data favours the structure for the heptaphyrin, **20**, as shown in scheme 6, wherein one of the *meso* phenyl ring is inverted and is in the ring current region of the macrocycle. Apart from that the central ring of the tripyrrole is also inverted and the ***b***-substituents are found to resonate in the up field region at –4·2 ppm. But the crystal structure of the heptaphyrin is in sharp contrast to the solution structure data. In the solid state, **20**, exhibits a figure of eight conformation consisting of a three-membered unit and a four-membered unit. This difference in the solution state and the solid state structures is explained based on the dynamism between the two enantiomeric forms of the macrocycle. In solution state, an averaged out spectrum for both the enantiomeric forms is observed and hence a flat structure has been proposed in solution. The structure observed in the solid state is purely due to the crystal packing effects and not due to crystallization of a specific isomer. Even though, solution state analyses exhibit up field signals indicating the ring current effect, it has not been accounted in the solid state. Thus a sort of pseudo-aromatic character has been observed for the first time in the case of expanded porphyrins. To date, a solid state proof for the aromaticity of 30***p*** heptaphyrins still haunts the expanded porphyrin chemists, even though such a proof has already been published for its higher congener, the 34***p*** octaphyrin.[14]

3. Conclusions

In general, expanded porphyrins having more than six heterocyclic rings can also be designed to sustain aromaticity as described above. The easy synthetic methodologies that have been developed using stable precursors, demonstrate that clever modifications of the precursors is one of the important tool in accessing higher aromatic expanded porphyrins. The substituent effect of the *meso* carbon can be tuned to enlarge the porphyrin core with suitable oligomers of the heterocyclic rings. The structure diversity in terms of ring inversions, the effect of bulkier *meso* substituents on the nature of products formed and the effects of aromaticity on the nature of bridging *meso* carbons need to be understood further in order to design appropriate expanded porphyrins for specific applications. Studies in this direction are in progress.

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