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NOTE

Largest Aromatic Nanoring*

According to Hückel's rule, cyclic planar molecules having a delocalized conjugated π-system containing $4n + 2$ π-electrons are aromatic.[1] Typically aromatic molecules undergo electrophilic aromatic substitution but not electrophilic addition reactions characteristics of molecules containing isolated double bonds. The simplest example of an aromatic molecule is benzene. Antiaromaticity (also known as Baird aromaticity) is observed in cyclic and planar molecules having $4n$ π-electrons. Cyclobutadiene is an example of the antiaromatic compounds. There are exceptions to the $4n$ rule. For example, molecules like pyrene (16 π-electrons) and coronene (24 π-electrons) having $4n$ π-electrons are aromatic. Compounds that do not fall into these two categories are nonaromatic. Hückel's rule of aromaticity applies to such molecules with $4n + 2$ π electrons in their singlet ground state, S_0. In contrast, Baird's rule of aromaticity applies to molecules with $4n$ π electrons in their lowest triplet state, T_1. Benzene is aromatic in the ground state (S_0) but antiaromatic in its excited state (T_1). The antiaromatic molecules in their excited state lose planarity and become nonaromatic.[2]

The aromaticity of a molecule is best determined by the proton NMR spectra of the molecule. In NMR spectroscopy, the molecule in a suitable NMR solvent is subjected to a strong external magnetic field. In this field, the circulating π-electrons of the molecule produce a diatropic ring current called *aromatic ring current*[3,4] in a specific direction. This ring current induces a magnetic field of its own. The direction of the induced magnetic field is the same as the direction of the applied magnetic field outside the π-electron ring, but it is opposite inside the ring. Hence protons outside the ring are deshielded, and those inside the ring get shielded (Figure 1). In benzene, there are six protons outside the π-ring and no protons inside. The ^{1}H NMR spectrum of benzene shows the magnetically and chemically equivalent protons present outside the π-ring at 7.33 ppm, further downfield the alkene protons, which appear between 4.5-6.5 ppm.

A clear demonstration of aromaticity by NMR requires a molecule having protons both outside and inside the π-electron ring, such as the annulenes.[5] [18]Annulene (cyclooctadecanonaene) has 12 protons outside the 18 π-electron ring and 6 protons inside. The ^{1}H NMR spectra of [18]annulene taken in THF-d_8 at −60 °C shows a 12H signal at 9.25 ppm and 6H signal at −2.9 ppm. Aromaticity is temperature-dependent. The proton NMR spectra of [18]annulene recorded at 120 °C shows a single signal at 5.45 ppm, which is the weighted average of the two individual signals. At elevated temperatures, there is a rapid exchange of the exterior and interior hydrogens.

For antiaromatic compounds, the ring current is paratropic, and its direction is opposite that of the aromatic compounds. Consequently, the direction of the induced magnetic field inside the ring is the same as the applied magnetic field. The proton NMR pattern is reversed, *i.e.*, the protons outside the ring are shielded, and those inside the ring are deshielded. The dianion of [18]annulene (20 π-electrons) is antiaromatic. Its inner protons are strongly deshielded at 20.8 ppm and 29.5 ppm, and the outer protons are significantly shielded at −1.1 ppm. Porphyrins have 18 π-electrons in a planar, continuous cycle.[6] The substructure of the molecule resembles that of [18]annulene. The two π bonds outside the 18 π-electron ring (Figure 2) have significant double bond character. The ^{1}H NMR spectra of porphyrins show that the external *meso*-protons resonate downfield near 10 ppm while the internal NH protons give a broad peak near −4.0 ppm. The diatropic ring current of porphyrins results in a highly deshielded external C−H protons while the inner N−H protons are strongly shielded.

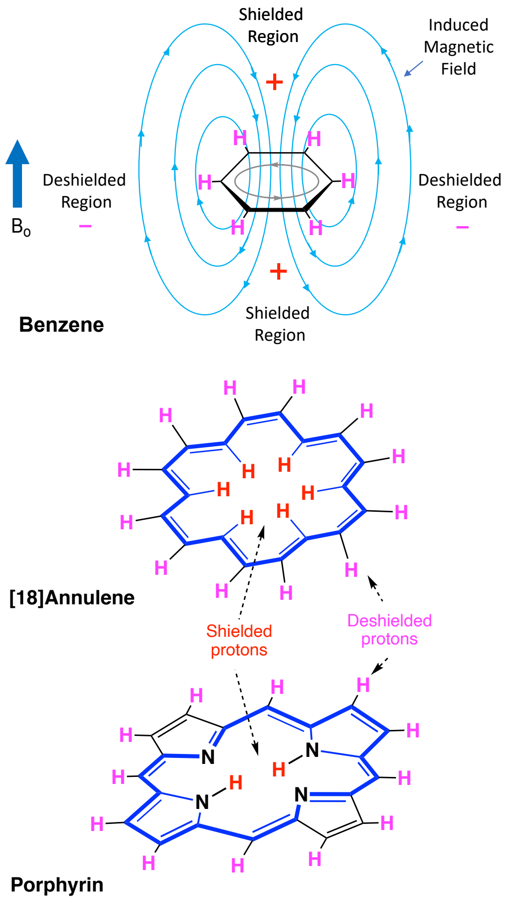

Figure 1. In the NMR environment, the directions of the induced magnetic field inside and outside the π-electron ring of benzene, [18]annulene, and porphyrin, causing shielding and deshielding effects.

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* *Contributed by* S. Samal, Editor, CSR

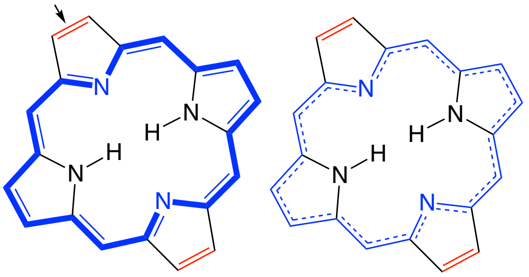


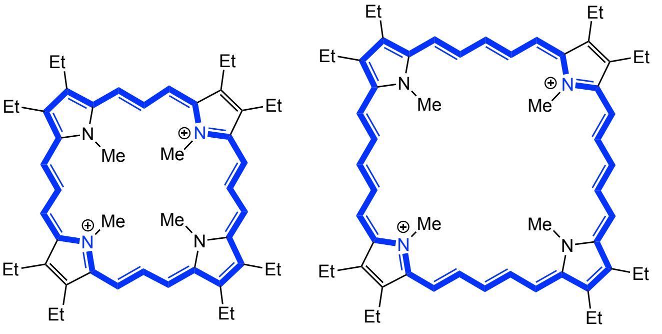
Figure 2. Structure of porphyrin showing the π bonds outside the 18 π-electron ring, which have significant double bond character.

The [*n*]annulenes, depending on the number of π-electrons in the ring, are aromatic, antiaromatic, weakly aromatic, weakly antiaromatic, or nonaromatic (Table 1). The chemical shift for the protons inside [12]annulene ring is 5.91 ppm, and that for the protons outside the ring is 7.86 ppm. Hence, the molecule is weakly antiaromatic. [10]Annulene has 10 π-electrons in a cyclic system, and according to Hückel's rule, it should be aromatic. The molecule is *not* aromatic, because ring strains destabilize an all-planar geometry. [8]Annulene (cyclooctatetraene), with 8 π-electrons should be antiaromatic, but it has a tub-like structure (non-planar) and hence not aromatic. On the other hand, the dianion of [8]annulene ($C_8H_8^{2-}$) having10 π-electrons is planar and aromatic.

Table 1. *Aromaticity* of [*n*]annulenes and the number of π-electrons in the ring.

n	**Aromaticity**
4	antiaromatic
6	aromatic
8	nonaromatic
10	nonaromatic
12	weakly antiaromatic
14	weakly aromatics
16	weakly antiaromatic
18	aromatic

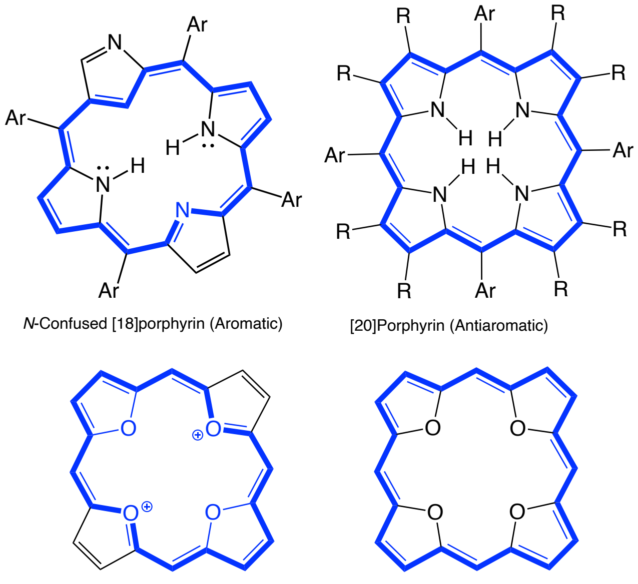
The difference between the deshielded and shielded proton resonances (Δδ) is a measure of the extent of aromaticity or antiaromaticity. ^{1}H NMR studies on a series of vinylogous porphyrinoids, including [26]porphyrin[3.3.3.3] and [34]porphyrin[5.5.5.5] (Figure 3),[7, 8] demonstrated that these systems obey Hückel's rule for aromaticity. The [34]porphyrin exhibits an extraordinarily large ring-current effect in the ^{1}H NMR spectrum. The inner bridging C–H protons give resonance signal at −14.27 ppm, and the internal methyl group protons give rise to a 12H singlet at −11.44 ppm. In comparison, the outer vinylogous protons register a doublet and a triplet at +16.18 and +17.19 ppm. This corresponds to a remarkable difference between the upfield and downfield proton resonances (Δδ) of ~31.5 ppm. The diamagnetic ring-current effect of [34]porphyrin significantly surpasses that of [26]porphyrin (Δδ = 25.3 ppm) and [18]annulene (Δδ = 12.1 ppm). The high ring-current effect of [26]porphyrin and [34]porphyrin characterizing aromaticity support the 4*n* + 2 rule for higher annulene systems. Several aromatic and antiaromatic porphyrin analogs (Figure 4) are shown to obey Hückel's rule. The *N*-confused [18]porphyrin, in which a pyrrole unit is connected to the rest of the ring through α,β'-linkage, is aromatic, while the [20]porphyrin is antiaromatic. The tetraoxaporphyrin is antiaromatic, whereas its dication is aromatic.



[26]Porphyrin[3.3.3.3]

[34]Porphyrin[5.5.5.5]

Figure 3. Structures of vinylogous porphyrinoids, [26]porphyrin[3.3.3.3] and [34]porphyrin[5.5.5.5]. Adapted from Reference [8], T. D. Lash, Origin of aromatic character in porphyrinoid systems. *J. Porphyr. Phthalocyanines* **2011**, *15*, 1093-1115. Copyright © 2011 World Scientific Publishing Company.



N-Confused [18]porphyrin (Aromatic)

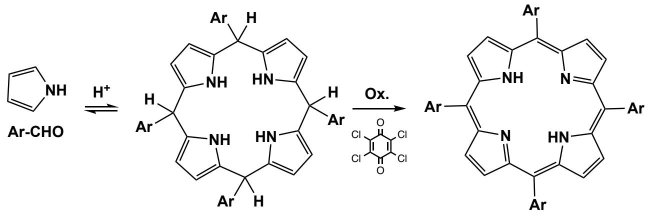
[20]Porphyrin (Antiaromatic)

Tetraoxaporphyrin dication (Aromatic)

Tetraoxaporphyrin (Antiaromatic)

Figure 4. Aromatic and antiaromatic porphyrin analogues.

A large variety of *meso*-aryl-substituted expanded porphyrins are obtained in good yield following the modified Lindsey method.[9] In this method (Scheme 1), pyrrole and aryl aldehyde are allowed to react at room temperature in dry CH_2Cl_2 under N_2 with a trace of an acid catalyst (BF_3 or trifluoroacetic acid). The reaction is reversible under these conditions. After the system reaches equilibrium, a stoichiometric amount of *p*-chloranil (2,3,5,6-tetrachlorobenzoquinone) or DDQ (2,3-dichloro-5,6-dicyanobenzoquinone) is added to oxidize the tetraarylporphyrinogen to porphyrin irreversibly.



Scheme 1. Lindsey method for synthesis of aryl-substituted porphyrins. Adapted from Reference [9], Lindsey *et al.*, Synthesis of tetraphenylporphyrins under very mild conditions. *Tetrahedron Lett.* **1986**, *27*, 4969-4970. Copyright @ 1986 Pergamon Journals Ltd.

The yield is critically dependent on the reactant concentrations. With benzaldehyde and pyrrole at 10^{-2} M, the yield of porphyrin is 46%. The yield is 14% at 10^{-1} M and 16% at 10^{-3} M. Under the modified Lindsey conditions, both the reactants were taken at a relatively high concentration of 67 mM in CH_2Cl_2 with 4.2 mM $BF_3.OEt_2$. In these conditions, a mixture of new *meso*-aryl-substituted expanded porphyrins was obtained. After the oxidation with DDQ, repeated chromatography led to the isolation of porphyrin (11~12%), pentaphyrin (14~15%), hexaphyrin (16~20%), heptaphyrin (4~5%), octaphyrin (5~6%), nonaphyrin (2~3%), and even higher homologs.

With an increasing number of pyrrole units, some pyrrole units were inverted. The rings became deformed and often twisted, adopting the Möbius conformation. The X-ray crystal structure of the octaphyrin shows a twisted figure-eight conformation with near C_2 symmetry, consisting of two porphyrin-like hemi-macrocycles. The ^{1}H NMR spectrum of the octaphyrin shows a C_2 symmetric signal pattern containing four pairs of doublets of the pyrrolic β-Hs in 7.67-6.11 ppm and two broad signals of the inner NHs at 13.25 and 8.59 ppm implying its nonaromatic nature. The nonaphyrin has 42 π-electrons. ^{1}H NMR also shows C_2 symmetric signals but with markedly different chemical shifts, particularly for the β-pyrrolic protons suggesting the aromatic electronic character.

Quantitative and reversible switch between a Hückel aromatic molecule and a Möbius aromatic molecule is demonstrated in the redox interconversion of [26]hexaphyrin and [28]hexaphyrin (Figure 5).[10] The [28]hexaphyrins (1.1.1.1.1.1) in solution at 25°C exist as an equilibrium among several rapidly interconverting Möbius structures each with aromatic character. In the solid-state, the molecules take either planar or Möbius conformations, depending on the aryl substituent and solvent used. When the temperature is decreased to −100°C, rapid interconversions among the conformations get frozen, leading to a single Möbius species.

Depending upon the number of π-electrons and the molecular topology, the expanded porphyrins may be either Hückel aromatic, Hückel antiaromatic, Möbius aromatic, or Möbius antiaromatic. A [46]decaphyrin bridged internally by 1,4-phenylene and a core-modified [40]octaphyrin represent the Hückel aromatic and antiaromatic molecules, respectively.[11] The *bis*-Pd^{II} [36]octaphyrin complex and phosphorus [34]heptaphyrin complex are respectively the Möbius aromatic and antiaromatic molecules. With increasing ring size, geometric disorder increases. To get molecules of ordered conformations, various strategies, such as internal bridging (Figure 6), and using templates, were adopted. Studies on annulenes have led to the conclusion that aromaticity decreases with increasing ring size and vanishes for systems with more than 30π electrons, which corresponds to a diameter of 1.3 nm. However, aromaticity can be preserved in large systems if the geometric disorder is suppressed.

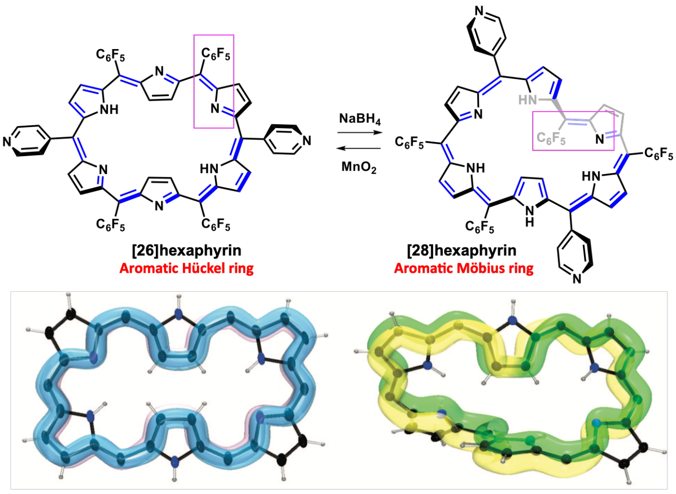


Figure 5. Conversion of [26]hexaphyrin, an aromatic Hückel ring, by reduction to [28]hexaphyrin having an aromatic Mobius structure. Adapted from Reference [10] with permission, Sankar *et al.*, Unambiguous identification of Mobius aromaticity for meso-aryl-substituted [28] hexaphyrins (1.1. 1.1. 1.1). *J. Am. Chem. Soc.* **2008**, *130*, 1568-13579. Copyright @ 2008 American Chemical Society.

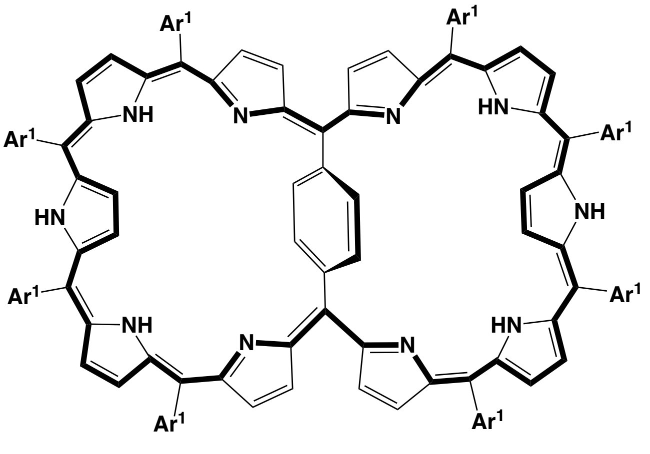


Figure 6. [46]Decaphyrin bridged internally by 1,4-phenylene. Adapted from Reference [11], Yoneda *et al.*, Pd^{II} Complexes of [44]- and [46] decaphyrins: the largest Hückel aromatic and antiaromatic, and Möbius aromatic macrocycles. *Angew. Chem. Int. Ed.* **2014**, *53*, 13169-13173. Copyright © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

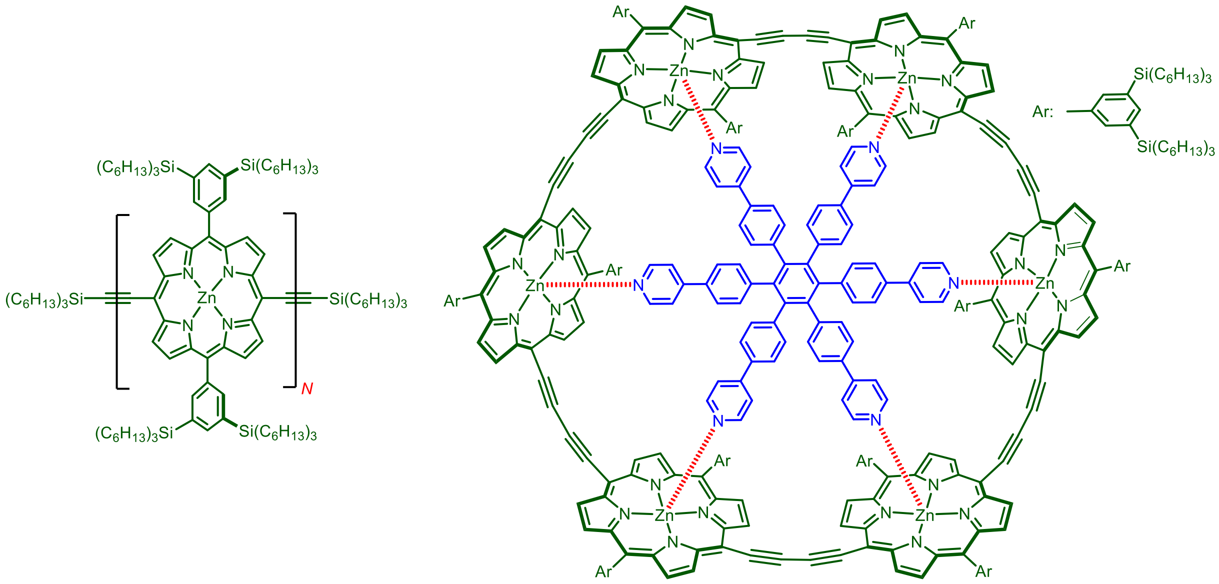


Figure 7. Butadiyne-linked porphyrin oligomer, the precursor for the six porphyrin nanoring and stabilized by a template made of central benzene in a six-legged structure with 4-pyridyl ends. Redrawn adapting the structure from Reference [13], Peeks *et al.*, Aromatic and antiaromatic ring currents in a molecular nanoring. *Nature* **2017**, *541*, 200-203. Copyright © 2017 Nature Publishing Group.

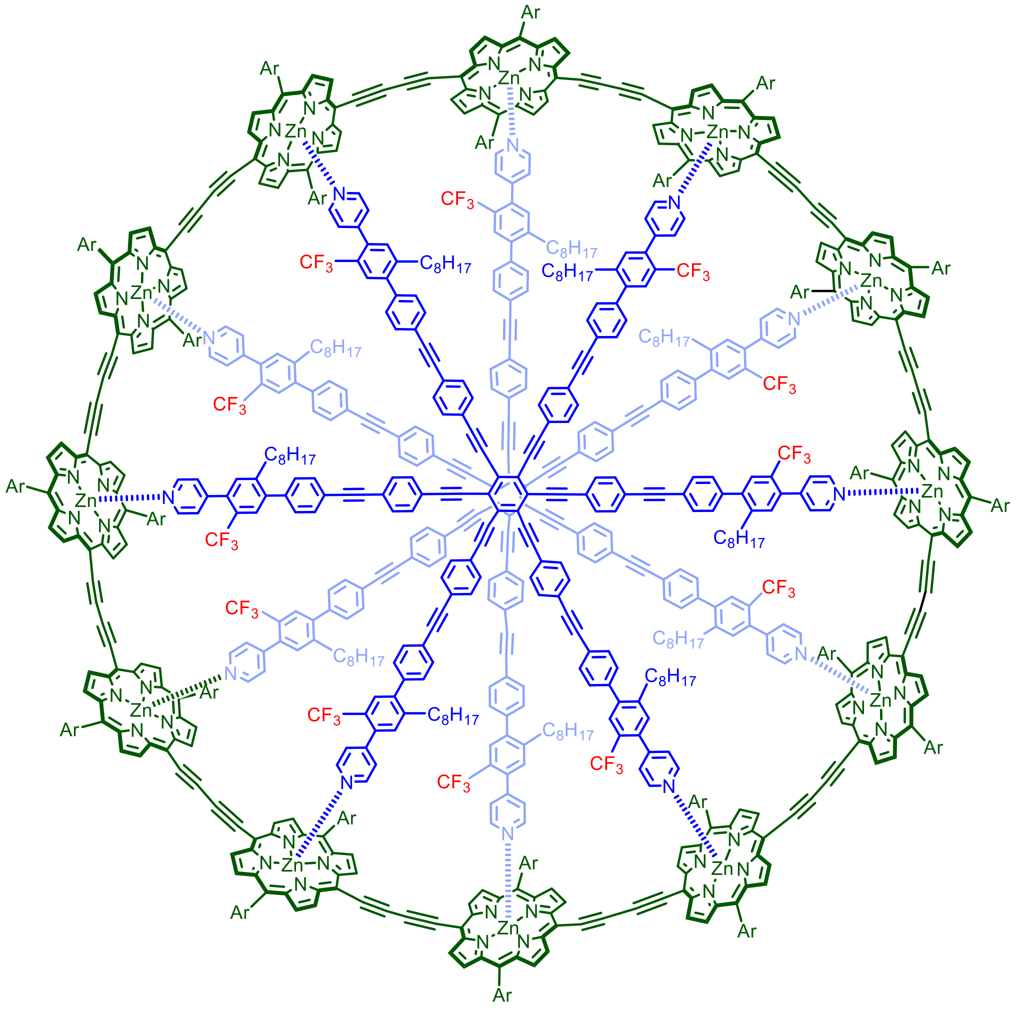


Figure 8. Porphyrin nanoring with 12 porphyrin units forming the largest known aromatic species. Redrawn adapting the structure from Reference [16], Rickhaus *et al.*, Global aromaticity at the nanoscale. *Nat. Chem.* **2020**, *12*, 236-241. Copyright © 2020 Nature Publishing Group.

Large, stable Hückel aromatic molecules [48]-, [50]-dodecaphyrins(1.1.0.1.1.0.1.1.0.1.1.0) were accessible from aromatic [52]dodecaphyrins(1.1.0.1.1.0.1.1.0.1.1.0).[12] The 50π dodecaphyrin has a size of 1.3 nm, and still, the aromaticity was retained. Even larger aromatic molecules from butadiyne-linked porphyrin oligomers were accessible by a template method (Figure 7).[13] The six porphyrin nanoring template complex with a diameter of 2.4 nm is antiaromatic in its 4+ oxidation state (80 π-electrons) and aromatic in its 2+ and 6+ oxidation states, with 82 and 78 π-electrons, respectively. The work demonstrates that a global ring current can be promoted in a macrocycle by adjusting its oxidation states to suppress the local ring currents of its components. Evidence for ring currents comes from the chemical shifts of the template α- and β-pyridyl ^{1}H resonances. In the free template, the α- and β-pyridyl ^{1}H resonances appearing at 8.7 and 7.5 ppm, respectively, are deshielded. These protons in the 2+ oxidation state of the porphyrin nanoring (aromatic) are strongly shielded, showing resonances at −7.3 and −3.6 ppm, respectively. In the 4+ oxidation state (antiaromatic), the protons are strongly deshielded, with the proton resonances appearing at 36.0 and 30.1 ppm, respectively.

The aromaticity of π-conjugated organic molecules is not restricted to 2D systems. The global aromaticity in 3D π-conjugated molecules, such as in [60]fullerene, is also reported in a fully conjugated non-fullerene molecular cage at different oxidation states.[14] The neutral compound with 38π monocyclic conjugation pathway follows the $4n + 2$ Hückel aromaticity rule. The dication with 36π conjugation satisfies $4n$ Baird aromaticity. The tetracation with 52 π-electrons and the hexacation with 50 π-electrons are delocalized along the 3D rigid framework, showing 3D global antiaromaticity.

Until recently, the largest aromatic molecule known was [62]tetradecaphyrin and its Zn^{II} complexes.[15] The *bis*-Zn^{II} complex showed moderate aromatic character as the largest Hückel aromatic molecule reported. Concurrently, porphyrin nanorings with 8 and 12 porphyrin units, molecules a lot larger than the [62]tetradecaphyrin, are reported (Figure 8).[16] Evidence for global aromaticity in such large rings is illustrated by the ^{1}H NMR spectra of the nanoring complex from 8 porphyrins with a circuit of 96 π-electrons when neutral. The template protons show clear evidence for aromaticity in the 2+ and 6+ oxidation states, but the 4+ ad 8+ states are antiaromatic.

Larger porphyrin nanorings having 12 porphyrin units are made using an extended six-legged template. Two molecules of this template stack to form a stable 2:1 complex leading to the 12-porphyrin nanoring having a diameter of ~5.0 nm. It has a circuit of 162 π-electrons when neutral. To probe the ring current, ^{19}F NMR was used. In the aromatic 6+ and 10+ oxidation states, the CF$_3$ ^{19}F resonances are shielded but deshielded in the antiaromatic 8+ oxidation state.

It is still not clear whether aromaticity has a size limit, or whether Hückel's rule extends to still larger macrocycles. Hückel's rule was formulated to explain the unusual properties of benzene and other molecules with 6 π-electrons. The simple rule correctly predicts the magnetic response of large, oxidized nanorings of up to 162 π-electrons, the largest aromatic species thus far known.

August Kekulé and Erick Hückel and benzene enigma continues!

Friedrich August Kekulé (1829–1896), German organic chemist, is well-known for the Kekulé structure of benzene. The world owes to August Kekulé for our present understanding of benzene (and hence of all aromatic compounds) proposed in 1865.[17] In 1890, the German Chemical Society celebrated the twenty-fifth anniversary of first benzene paper. Speaking on this occasion, Kekulé said that he had discovered the ring shape of the benzene molecule after having a dream of a snake seizing its own tail.

Erick Hückel (1896-1980) was born in Berlin. He studied from 1914 to 1921 at the University of Göttingen. On receiving his Ph.D. he became an assistant to Peter Debye. It was here in 1923 that Hückel and Debye developed their famous Debye–Hückel equation. After this, Hückel joined the faculty of the University of Stuttgart. In 1935, he moved to the University of Marburg where he became a Full Professor a year before his retirement in 1961. The Hückel theory, that cyclic systems with $4n + 2$ π-electrons exhibit aromatic stability, was first articulated by William Doering (1917-2011), a Professor Emeritus at Harvard University and the former Chair of its Chemistry Department. A simple rule that successfully explained the aromaticity of molecules to date started its course from benzene.

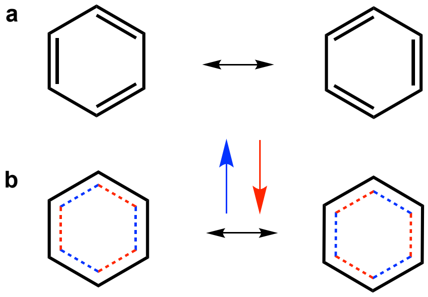


Figure 9. Resonance in benzene. (a) The classical Kekulé structures. (b) A pictorial description of benzene structure. Different electron spins are colored red and blue. Redrawn adapting the structure from Reference [18], Liu *et al.*, The electronic structure of benzene from a tiling of the correlated 126-dimensional wavefunction. *Nat. Commun.* **2020**, *11*, 1210. Copyright © 2020 Nature Publishing Group.

Over 150 years after Kekulé proposed the structure of benzene, debates are still on as to what could be the actual structure of benzene. The valence bond theory is based on localizing electrons within resonance structures, and molecular orbital theory describes delocalized electrons. Schmidt and co-workers re-examined the structure of benzene (Figure 9)[18] from the principal effect of electron correlation and concluded that electrons would not be spatially paired when it is energetically advantageous to avoid one another! This work underlines that a complete qualitative description of electronic structure, where resonance is exhibited, requires the unpairing of spins.

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