Macrocyclic Conjugation Pathways in Porphyrins

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Macrocyclic aromaticity is the most important concept in porphyrinoid chemistry. Bond resonance energy (BRE) for any π-bond linking adjacent pyrrolic or other rings represents the stabilization energy due to macrocyclic aromaticity. We found that a main conjugation pathway associated with macrocyclic aromaticity can be traced by choosing a π-bond with a larger BRE at every bifurcation of the π-network. All π-bonds located along the main conjugation pathway are intensified with large positive BREs compared with those located along the bypasses. On the other hand, a main destabilization pathway associated with macrocyclic antiaromaticity can be traced by choosing a π-bond with a smaller BRE at every bifurcation of the π-network. Macrocyclic conjugation pathways thus determined are fully consistent with the chemical shifts of protons attached to the macrocycle.

Introduction

Free-base porphine has been described as bridged diaza[18]-annulene with two localized β-β' pyrrolic double bonds.[1–3] This conjugation or delocalization picture emphasizes that an 18-π conjugation pathway must contribute predominantly to the aromaticity of porphine. Lash often calls the porphyrins Nature's [18]annulenes,[3] which emphasize that they constitute an unparalleled family of aromatic macrocycles that formally possess [18]annulene characteristics and as such are the only naturally occurring examples of higher bridged annulene structures. The principal ring current is then supposed to circulate around the outside of two pyrrole rings and around the inside of the other two. This viewpoint has been supported primarily by the planarity of the molecule and the down- and upfield chemical shifts of the outside and inside perimeter protons, respectively.[1–3]

At the turn of the century, three research groups reinvestigated possible aromatic pathways of free-base porphine and metalloporphine in detail.[4–8] They all noted that not only conjugation along the porphyrin macrocycle but also local aromaticity in individual pyrrolic rings is important in determining the global aromaticity of porphyrins. We also explored possible aromatic conjugation pathways in free-base porphine and metalloporphine[9] using our graph theory of aromaticity.[10–23] It was found that the macrocyclic conjugation pathway contributes significantly to proton and nucleus-independent chemical shifts but much less to the thermodynamic stabilization of the entire π-system.[9] The main origin of global aromaticity proved to be individual pyrrolic rings.

Nevertheless, macrocyclic aromaticity has remained the central concept of porphyrin chemistry. Many studies have focused upon the aromatic characteristics of macrocyclic oligopyrroles. Porphyrin chemists applied Hückel's $(4n + 2)$ rule not only to other tetrapyrrolic macrocycles but also to a variety of confused and expanded porphyrins.[1–4,24–29] They refer to macrocyclic aromaticity simply as aromaticity. It seems likely that the kinetic stability and magnetic properties of many porphyrinoid species are determined by the macrocyclic conjugation even if it is not a determinant of global aromaticity.[1–3,24–29] Franck proposed that porphyrinoid species should be grouped according to the number of π-electrons in the shortest macrocyclic conjugation pathway.[2] In this study, we explore macrocyclic conjugation pathways and extra stabilization energies due to macrocyclic conjugation in a variety of porphyrinoid species using our graph theory of aromaticity.[10–23]

Theory

Our graph theory of aromaticity is formulated within the framework of the simple Hückel molecular orbital theory.[10–23] As stated explicitly by Dewar and others,[30–32] the term "aromatic" describes molecules that benefit energetically from the delocalization of mobile electrons in closed circuits. In our theory, topological resonance energy (TRE) is used as an energetic criterion of global aromaticity.[10–12] Van-Catledge's set of Hückel parameters for heteroatoms[33] is employed throughout this study. Possible deformation of a porphyrinoid π-system is not taken into consideration.

Bond resonance energy (BRE) is defined as follows.[15–17] A hypothetical π-system, in which a given π-bond (e.g., a π-bond formed between the pth and qth atoms) interrupts cyclic conjugation thereat, is constructed by multiplying β_{pq} by i and β_{qp} by $-i$, where β_{pq} is the resonance integral between the two conjugated atoms and i is the square root of -1. In this π-system, no circulation of π-electrons is expected along the circuits that share the p−q π-bond in common. The BRE for the p−q π-bond is given as a destabilization energy of this hypothetical π-system. In other words, the BRE for a given π-bond represents the contribution of all circuits that share the bond to TRE.[15–17] This quantity was originally defined to justify the isolated pentagon rule for fullerenes.[15] Recently, we found that BRE can also be used as an indicator of local aromaticity for a polycyclic π-system.[18]

Peripheral π-bonds have the same BRE value if they belong to the same ring. BRE vanishes for olefinic π-bonds. The BRE for a peripheral π-bond will be referred to as a peripheral BRE. If the minimum BRE in a molecule is smaller than $-0.100\,|\beta|$, then it is highly probable that the molecule is kinetically very unstable.[15–17] Superaromatic stabilization energy (SSE) represents extra stabilization energy due to macrocyclic conjugation.[13,14] It constitutes part of TRE. For all porphyrinoids, the SSE is equal to the BRE for any of the CC bonds that link pyrrolic and/or phenylene rings.[14] BREs for all these π-bonds are the

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same in magnitude. We hereafter use the term "macrocyclic aromaticity" as a synonym of the term "superaromaticity".

Results and Discussion

There are many different porphyrinoid species, including regular, contracted, confused, inverted, and extended porphyrins.[1–3,24–29] We first examine the aromatic character of 20 free bases and one metalloporphine, all with a 16-atom internal cross. Structural formulas of these porphyrinoids are shown in Figure 1, together with the BREs for all nonidentical π-bonds. Table 1 contains the TREs and SSEs for these porphyrinoids. In many of them, one or more of the internal nitrogen atoms are replaced by carbon atoms. TREs for all these species are positive in sign irrespective of the sign of the SSE, indicating that the entire π-system is more or less stabilized by cyclic conjugation. Two of them, dihydroporphyrin (**2**) and didehydroporphyrin (**3**), have relatively small positive TREs. As will be seen below, these two species are very reactive.[34,35] Many porphyrinoids have positive SSEs, indicating the presence of macrocyclic aromaticity.

Free-base porphine or porphyrin (**1**) has a positive TRE comparable to that of tricyclic anthracene (TRE = 0.4746 $|\beta|$).[9] For all but **2** and **3**, the TRE per pyrrolic ring is ca. 0.10 $|\beta|$, indicating that the aromaticity of the isolated pyrrole molecule is greatly suppressed by cross conjugation in the porphyrinoid species. The TRE for pyrrole is 0.2462 $|\beta|$.[10–12] Even for **2**, part of the TRE due to four pyrrolic rings is predicted to be more than 0.40 $|\beta|$, because the SSE has an exceptionally large negative value. Thus, most of the porphyrinoids, including **1**, are not highly but moderately aromatic. In general, the SSE for a porphyrinoid macrocycle, that is, the BRE for any of the CC bonds that link pyrrolic rings, is fairly small. For example, the SSE for **1** (0.0843 $|\beta|$) amounts only to 17% of the TRE even though it is not negligibly small. It follows that the [18]annulene-like conjugation pathway in porphyrinoid species is not crucial for determining the aromaticity of the entire π-system.[9] For reference, the TRE for [18]annulene is 0.0877 $|\beta|$.

The main aromatic conjugation pathways proposed by porphyrin chemists are shown in bold in Figure 1. Most of them are the smallest macrocyclic conjugated circuits in Randić's terminology.[36] The BREs corresponding to the SSEs are indicated with bold underlines. Porphyrinoid macrocycles with positive SSEs are aromatic in the Hückel sense; that is, the macrocycle contains a closed circuit (delocalization pathway) along which $4n + 2$ π-electrons reside. Free-base porphine (**1**) itself contains an 18-atom, 18-π-electron pathway. This molecule has no explicit antiaromatic substructures; all π-bonds have positive BREs, contributing more or less to the aromaticity of an entire π-system. For many porphyrinoid species, π-bonds in pyrrolic rings exhibit larger BREs than do the π-bonds linking these rings, supporting the view that these subunits are the main source of global aromaticity.[9]

One should note that a main macrocyclic conjugation pathway in **1** consists of π-bonds with larger BREs than bypass π-bonds. The same is true for all porphyrinoid species with positive SSEs. This fact indicates that the aromatic conjugation pathway can be traced without ambiguity by choosing a π-bond with a larger BRE at every bifurcation of the π-network. Thus, BREs are useful for identifying an aromatic conjugation pathway in porphyrinoids and, conversely, support the existence of such a pathway in porphyrinoid species. This never implies that macrocyclic conjugation dominates global aromaticity.

Porphyrinoids containing $4n$-π-electron pathways, which are expected to show antiaromatic behavior, are less common. Woodward, in the course of his ingenious chlorophyll synthesis, pointed out that isophlorin (dihydroporphyrin, **2**) is a true non-Hückel [20]annulene and anticipated it to be very prone to oxidation to porphyrin.[43] This molecule is predicted to exhibit macrocyclic antiaromaticity with the largest negative SSE. The ^{1}H NMR spectrum of tetramethylisophlorin suggests that the heterocyclic five-membered rings are alternately of pyrrole- and pyrroline-type with localized π-bonds and can be interpreted reasonably in terms of the almost complete conformation-induced loss of the paratropicity in the macrocycle.[34] Bond localization was also observed in silicon isophlorin.[44] In this case, an antiaromatic conjugation pathway consists of π-bonds with negative or relatively small positive BREs.

Didehydroporphyrin (**3**) contains an antiaromatic 16-π-electron pathway. This conjugation pathway runs along the 16-atom internal cross and represents the only conjugated circuit in this molecule. The SSE is very large in magnitude but negative in sign. The TRE is very small due to the pronounced macrocyclic antiaromaticity, indicating that **3** is nonaromatic in any way. Experimentally, this macrocycle proved to be nonaromatic due to the pronounced bond-length alternation and the distortion of the macrocycle caused by bulky peripheral substitution.[35]

Carbaporphyrin (**4**),[37,38] confused porphyrin (**5**),[38–41] and doubly N-confused porphyrin (**7**)[41] are all iso-π-electronic with **1**. Their ^{1}H NMR spectra are consistent with the 18-π aromatic character of these macrocycles. The SSEs for all these species are larger than 0.600 $|\beta|$. N-Confused porphyrin **5** coexists with **6** in solution as a result of rapid NH tautomerization.[38,41] Macrocyclic conjugation in **6** is formally disrupted by the confused pyrrole ring; this ring is not formally conjugated with the tripyrrolic brace. This aspect of the macrocycle is compatible with a fairly small SSE. The SSE for **6** is 0.0501 $|\beta|$, being close to the critical value for porphyrinoid aromaticity ($\approx$0.0500 $|\beta|$). As may be seen from Table 1, it seems that pronounced macrocyclic aromaticity is associated with the SSE $>$ 0.0500 $|\beta|$. Dipolar resonance structures, such as **6′** in Figure 2, must be more or less responsible for the observation of a weak diamagnetic ring current along the macrocycle.[41]

m-Benziporphyrin (**8**) has a *m*-phenylene ring in place of one of the pyrrolic rings.[45,46] As macrocyclic conjugation is disrupted by this ring, no macrocyclic conjugated circuit can be chosen from the π-system. In agreement with this, the SSE for **8** is extremely small (0.0085 $|\beta|$) although it is still positive in sign. In fact, the ^{1}H NMR spectrum is not consistent with the presence of any macrocyclic ring current.[45,46] The lack of macrocyclic aromaticity is also predicted for 2-hydroxypyriporphyrin (**9**),[47] 22-hydroxybenziporphyrin (**11**),[48] and 2-hydroxybenziporphyrin (**13**).[49] The SSE is smaller than 0.500 $|\beta|$ for all these species, although no bond-length alternation is not considered in the SSE calculation. Local aromaticity of the benzene or pyridine ring is instead retained in these systems.

Porphyrinoids with a phenolic ring, such as hydroxypyriporphyrin (**9**),[47] 22-hydroxybenziporphyrin (**11**),[48] and 2-hydroxybenziporphyrin (**13**),[49] are expected to undergo keto–enol tautomerization in solution. However, **9** and **13** exist solely as the keto isomers **10** and **14**, respectively.[47,49] These keto tautomers retain strongly diatropic characteristics, in accord with the SSEs $>$ 0.500 $|\beta|$. Only **11** coexists with the keto tautomer (**12**) in solution.[48] The paratropicity of **12** is evident from features of the ^{1}H NMR spectrum. The enol or phenolic form **11** is nonaromatic as a macrocycle but shows a local benzenoid aromaticity. Porphyrinoid aromaticity is then possible at the expense of losing the local aromaticity of the benzene ring. The TREs for **9** and **13** are comparable in magnitude with

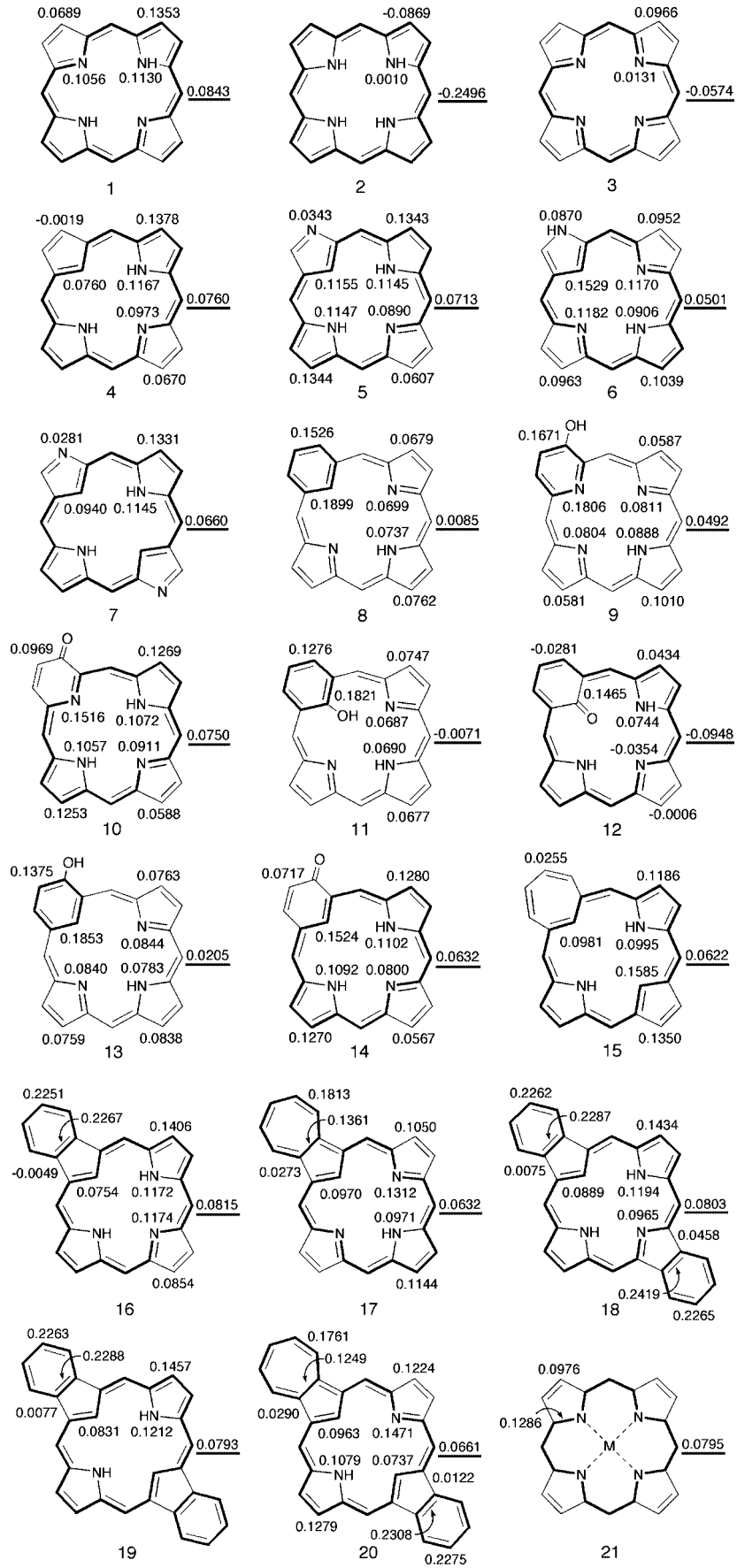

Figure 1. BREs in units of $|\beta|$ for 21 porphyrinoids with a 16-atom internal cross. SSEs are indicated with bold underlines.

those for **10** and **14**, respectively. However, the TRE for **11** is much larger than that for **12**, because the pronounced 20-π macrocyclic antiaromaticity of **12** contributes to the derease in the TRE. This must be why the two isomers coexist in solution.

TABLE 1: TREs and SSEs for Porphyrinoids with a 16-Atom Internal Cross

species	TRE/|β|	SSE/|β|
free-base porphine **1**	0.4322	0.0843
isophlorin **2**	0.2225	−0.2496
3	0.0602	−0.0574
4	0.3820	0.0760
5	0.4074	0.0713
6	0.4394	0.0501
7	0.3812	0.0660
8	0.3866	0.0085
9	0.3922	0.0492
10	0.4232	0.0750
11	0.3829	−0.0071
12	0.2513	−0.0948
13	0.4088	0.0205
14	0.4094	0.0632
15	0.4008	0.0622
16	0.6027	0.0815
17	0.4749	0.0632
18	0.7896	0.0803
19	0.7638	0.0793
20	0.5995	0.0661
metalloporphine **21**	0.4744	0.0795

Tropiporphyrin (**15**),[50] benzocarbaporphyrin (**16**),[51,52] dibenzocarbaporphyrin (**18**),[53] and *opp*-dibenzodicarbaporphyrin (**19**)[53] retain the main 18-π conjugation pathway with SSEs > 0.0500 |β|. The ^{1}H NMR spectra of **15** and **16** provide evidence for porphyrinoid aromaticity. Local tropylium ion character expected for **15** is suppressed effectively by macrocyclic conjugation.[50] The macrocyclic ring current is a bit greater in **18** than in **19**, possibly due to steric effects caused by the crowded cavity.[53] The SSEs are essentially the same for these two species. Benzene rings in **16**, **18**, and **19** are spatially separated from the main 18-π conjugation pathways. Therefore, these porphyrinoids exhibit not only pronounced porphyrinoid but also local benzenoid aromaticity.[51–53] All π-bonds in these benzene rings have very large BREs. Note that benzene has a TRE of 0.2726 |β|.[10–12]

Azulene is a typical nonbenzenoid aromatic hydrocarbon with a TRE of 0.1511 |β|.[10–12] Macrocyclic conjugation in azuliporphyrin (**17**) is formally disrupted by the azulene moiety, but there still is some possibility that local azulenoid and macrocyclic porphyrinoid aromaticity compete with each other.[54,55] This molecule was found to possesse a weak diatropic ring current, probably caused by a zwitterionic resonance contributor (**17′** in Figure 2).[54,55] This interpretation is consistent not only with the SSE > 0.0500 |β| but also with the large positive BREs for all π-bonds that constitute the tropylium ion ring. For reference, the TRE for the isolated tropylium ion is 0.2253 |β|. Dicarbaazuliporphyrin (**20**) also contains the azulene moiety, which again formally disrupts the macrocyclic conjugation, but the macrocycle is weakly diatropic.[55] In accord with this observation, the SSE for **20** is comparable in magnitude to that for **17**, suggesting that a dipolar canonical structure (**20′** in Figure 2) contributes somewhat to **20**.

For metalloporphines or metalloporphyrins, such as **21**, the 16-atom, 18-π inner conjugation pathway (i.e., an internal cross) with a formal charge of −2 has sometimes been viewed as a main origin of aromaticity.[4,6,8] The present BRE-based approach confirms that the internal cross is really a main macrocyclic conjugation pathway, along which π-bonds with relatively large BREs are arranged. This conjugation pathway is a main origin of macrocyclic aromaticity as supported by the SSE of 0.0795 |β|. Here, we assumed that all nitrogen atoms in **21** are of imine-type and that the central metal(II) ion does not participate in the porphyrin π-system.[9] The TREs for the [16]annulene dianion and dihydrotetraaza[16]annulene are 0.0968 and 0.0770 |β|, respectively. We did not examine the macrocyclic aromaticity of other charged or metalated porphyrins, because it is difficult to estimate the Hückel parameters for charged heteroatoms.

We next examine macrocyclic aromaticity in contracted and expanded porphyrins without a 16-atom internal cross. Structural formulas of 15 such porphyrinoids are shown Figure 3, together with the BREs for all nonidentical π-bonds. The TREs and SSEs for these species are listed in Table 2. Free-base porphine (**1**), on formal expulsion of a *meso*-methine unit, is converted into corrole (**22**), the basic ring framework of vitamin B_{12}. Like **1**, **22** features an 18-π main conjugation pathway bestowing macrocyclic aromaticity on the molecule.[56] Porphycene (**23**) is one of the most important structural isomers of **1**, which preserves an 18-π main conjugation pathway and macrocyclic aromaticity.[57,58] In accord with this, the SSEs for **22** and **23** are larger than 0.0500 |β|.

The [18]annulene character of many porphyrinoids in Table 1 implies the possible existence of their macrocyclic homologues, featuring $(4n + 2)\pi$ conjugation pathways.[1–3] Among such homologues of **1** and **22** might be **24**-**27**.[59–62] All of these tetrapyrrolic macrocycles have $(4n + 2)\pi$ conjugation pathways with SSEs > 0.500 |β|. The ^{1}H NMR *s*pectra demonstrate the macrocyclic aromaticity of these porphyrinoids.[59–62] Expanded porphyrins, such as sapphyrin (**29**)[63–65] and pentaphyrin (**30**),[66] likewise have $(4n + 2)\pi$ conjugation pathways with SSEs > 0.500 |β| and exhibit macrocyclic aromaticity. It is noteworthy that the SSEs for **29** and **30** are still larger than 0.500 |β|, although the macrocyclic conjugation pathways are larger than [18]annulene. Note that the larger $[4n + 2]$annulenes have smaller positive TREs. Both **26** and **27** have as large as 26-π conjugation pathways.

Di-*m*-benzihexaphyrin (**32**) does not possess overall macrocyclic aromaticity.[67] Macrocyclic conjugation in **32** is almost completely disrupted by two *m*-phenylene rings. This molecule necessarily lacks macrocyclic conjugated circuits. Like *m*-benziphyrins (**8**), which also lack macrocyclic conjugated circuits,[45,46] **32** has a vanishingly small SSE. Inner and outer

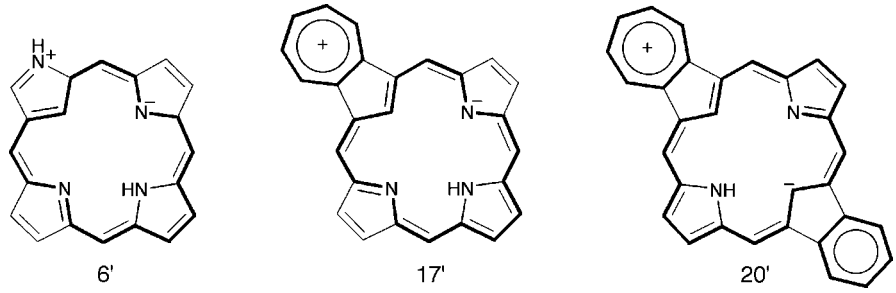

Figure 2. Example of dipolar resonance structures for **6**, **17**, and **20**.

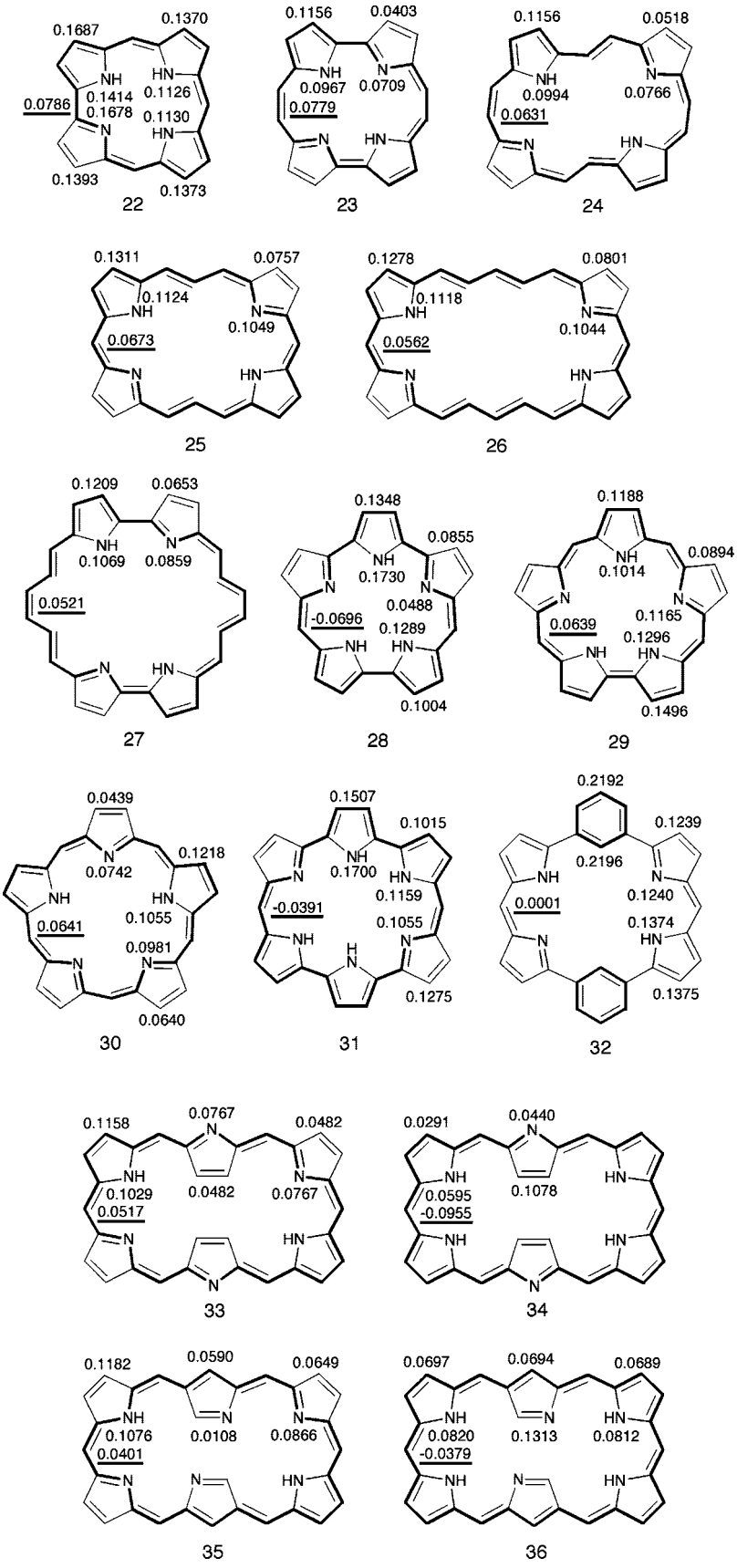

Figure 3. BREs in units of $|\beta|$ for 15 porphyrinoids without a 16-atom internal cross. The SSEs are indicated with bold underlines.

π-bonds of each pyrrolic and phenylene ring have essentially the same BREs, which also supports the view that none of the π-bonds constitute part of the macrocyclic conjugation pathway, if any.

Macrocyclic antiaromaticity must be easier to attain in expanded porphyrins, because larger antiaromatic pathways must be less antiaromatic. Orangarin (**28**), the smallest pentapyrrolic system, contains a 20-π conjugation pathway and so must

TABLE 2: TREs and SSEs for Porphyrinoids without a 16-Atom Internal Cross

species	TRE/|β|	SSE/|β|
corrole **22**	0.5688	0.0786
porphycene **23**	0.4862	0.0779
24	0.4744	0.0631
25	0.4367	0.0673
26	0.4375	0.0562
27	0.4904	0.0521
orangarin **28**	0.5656	−0.0696
sapphyrin **29**	0.5904	0.0639
30	0.4449	0.0641
amethyrin **31**	0.8020	−0.0391
32	0.9872	0.0001
33	0.4566	0.0517
34	0.5371	−0.0955
35	0.4422	0.0401
36	0.5992	−0.0379

exhibit macrocyclic antiaromaticity with an SSE of −0.0696 |β|. However, this macrocycle was found to be essentially atropic and hence nonaromatic.[65,68] Bond localization and the severely twisted bipyrrole moiety must be responsible for the nonaromatic nature.[65,68] Hexapyrrolic amethyrin (**31**)[68] has a 24-π antiaromatic conjugation pathway with a smaller negative SSE of −0.0391 |β|. The ^{1}H NMR spectrum of **31** is consistent with the presence of a global paramagnetic ring current.[68,69] As in the case of **2**, **3**, and **12**, the main antiaromatic pathways in **28** and **31** can be traced by choosing a π-bond with a smaller BRE at every bifurcation of the π-network.

Two hexaphyrins (**33** and **34**) and their doubly N-confused isomers (**35** and **36**) have been synthesized. The ^{1}H NMR spectrum of **33** displayed features consistent with the presence of 26-π macrocyclic aromaticity.[70] Doubly N-confused hexaphyrin **35** likewise has a 26-π aromatic conjugation pathway.[27,71] As the SSE for **35** is a bit smaller than the critical value we assumed for macrocyclic aromaticity (0.0500 |β|), the large area enclosed by the conjugation pathway concerned must be primarily responsible for the observable diamagnetic ring current. Note that the intensity of a ring currnet induced in a given circuit is proportional to the aromatic stabilization energy due to the circuit, multiplied by the area of the circuit.[9,19,20] By contrast, the ^{1}H NMR spectra of **34** and **36** reveal no indication of antiatomatic ring-current effects, although they have 28-π macrocyclic conjugation pathways with negative SSEs.[70,71] It is interesting to note that the TREs for **34** and **36** are larger than those for **33** and **35**, respectively, although the former species have paratropic macrocycles.

In fact, large macrocycles with negative SSEs, such as **34** and **36**, are often atropic, at least, in solution. The nonaromatic character of these species suggests that macrocyclic antiaromaticity, the degree of which tends to diminish upon going to larger macrocycles, can be suppressed easily by deforming a planar conformation of the macrocycle. In general, a macrocycle in a large porphyrinoid is very flexible in solution. Such an interpretation of the ^{1}H NMR spectra is fully consistent with the observation by Mori et al.[72,73] They noted that **34** becomes markedly paratropic when it is metalated with one or two Au(III) ions. It is evident that the planarity enforced by metalation is crucial to the appearance of antiaromaticity in large $4n$-π annulenoid pathways. Therefore, there is little doubt that macrocycles with negative SSEs are explicitly or potentially antiaromatic.

As has been seen, the present BRE-based approach to macrocyclic aromaticity proved to be very useful for establishing the concept of a main macrocyclic conjugation pathway in porphyrins and related species. If the SSE is positive in sign, then a main macrocyclic conjugation pathway can be determined uniquely by choosing a π-bond with a larger BRE at every bifurcation of the π-network. Conversely, a main pathway responsible for a negative SSE can be traced uniquely by choosing a π-bond with a smaller BRE at every bifurcation of the π-network. In other words, π-bonds located along an aromatic annulenoid pathway are all intensified with larger BREs than those located along the bypasses, whereas π-bonds located along an antiaromatic annulenoid pathway are weakened with smaller BREs. Macrocyclic conjugation pathways thus determined are fully supported by experimental chemical shifts of protons attached to the macrocycle. Such a macrocyclic conjugation pathway does not always correspond to a conjugated circuit in Randić's sense.[36]

The Hückel-like rule for macrocyclic aromaticity, confirmed in this study, can be extended to the molecular dianions and dications of all free-bases studied. If a neutral species has a positive SSE, then the dianion and dication will have negative SSEs. Conversely, if a neutral species has a negative SSE, then the dianion and dication will have positive SSEs. For many porphyrinoids, this Hückel-like rule can be extended to higher molecular ions. For example, SSEs for the molecular tetraanion, dianion, neutral species, dication, and tetracation of sapphyrin (**29**) are 0.0425, −0.1627, 0.0639, −0.0705, and 0.0621, respectively, all in units of |β|. It then follows that the doubly protonated species must retain the macrocyclic aromaticity of the parent porphyrinoid, whereas double hydrogenation must reverse the sign of macrocyclic aromaticity. The TRE decreases upon going to higher annulenes. Likewise, SSEs for heptaphyrins and octaphyrins[26] are all less than 0.500 |β|.

We recently found that the BRE for a given π-bond is nearly equal to the sum of circuit resonance energies (CREs) for all circuits that share the bond in common.[74] Here, the CRE indicates the contribution of each circuit to global aromaticity. Therefore, the SSE is nearly equal to the sum of CREs for all macrocyclic circuits.[9] For example, there are $2 \times 2 \times 2 \times 2 \times 2$ macrocyclic circuits in pentaphyrin (**30**). The SSE for **30** is close to the sum of CREs for the 32 macrocyclic circuits. A main macrocyclic conjugation pathway, determined experimentally and theoretically, corresponds to one of the macrocyclic circuits with the largest CRE. Therefore, it is very noteworthy that the BREs for the π-bonds situated along the main conjugation pathway are increased significantly. It is generally true that, for aromatic macrocycles, the smallest conjugated circuit has the largest CRE.

Concluding Remarks

It is very true that experimentally meaningful ideas, such as global and macrocyclic aromaticity, can often been justified theoretically. The annulene model for porphyrins may be an oversimplification, but it provides a useful conceptual framework in porphyrin chemistry.[50] In this paper, we confirmed in graph-theoretical terms the concepts of a main macrocyclic conjugation pathway and macrocyclic aromaticity closely associated with the annulene model. Macrocyclic antiaromaticity is one of the determinants in general porphyrin chemistry. Pyrrolic and phenylene subunits are aromatic in nature, whereas less aromatic *meso* carbon atoms are all under the sole influence of macrocyclic aromaticity/antiaromaticity. Note that the kinetic stability of a cyclic π-system is determined primarily by the reactivity of the most reactive site in the π-system.[15–17] In this sense, macrocyclic antiaromaticity, if any, is a determinant of kinetic

stability for porphyrinoids. Of course, macrocyclic conjugation contributes predominantly to the ring-current magnetism.[9] The present BRE-based approach would be useful for further deepening our understanding of macrocyclic aromaticity in a variety of known and unknown porphyrinoid species.

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