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Cyclic Conjugation in Porphin[+]

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The paper consists of three parts. In Part A the cyclic conjugation in porphin and some related compounds is examined. It is shown that the Hückel (4m+2)-rule is violated so that conjugation along both 16-, 17-, 18-, 19- and 20- membered cycles causes stabilization of the π-electron system of porphin. In Part B some comments on the topological resonance energy method and its application to porphin are given In Part C the four existing methods for the calculation of the effect of cyclic conjugation on the stability of π-electron systems are compared and their mutual relationship revealed.

PART A

EFFECT OF CYCLIC CONJUGATION ON THE THERMODYNAMIC STABILIY OF PORPHIN

INTRODUCTION

As it is well known[1], porphyrins and metalloporphyrins are among the most important natural products: iron-porphyrins form the prostetic groups of haemoproteins such as haemoglobins, cytochromes, catalases and peroxidases, whereas the chlorophylls are magnesium chelates of the closely related chlorins.

The parent compound of porphyrins is porphin (I), a fully conjugated 26 π-electron system containing a variety of cycles of size 16, 17, 18, 19 and 20. Hence, it is natural to expect that conjugation along these cycles will in a significant manner influence the physico-chemical (and therefore also biological) properties of porphyrins. A wealth of experiemntal evidence accumulated in the last decades confirming this viewpoint (see, in particular, references[1-6] and the papers cited therein).

In the last ten years the present author (in cooperation with a number of colleagues) developed a theory which enables the estimation of the effect of cyclic conjugation arising from any particular cycle of a conjugated molecule[7-12]. This approach is based on the mathematical formalism of graph theory[13] and is presently elaborated within the framework of the Hückel molecular orbital (HMO) model. The theory of cyclic conjugation can be used to analyze any π-electron property of a conjugated molecule, but is nowadays applied mainly to the study of the effect of cycles on total π-electron energy.

Although the π-electron energy constitutes only a smaller part of the total energy of a molecule, it is the crucial quantity for the understanding of the thermodynamic behaviour of conjugated compounds[5,14]. The π-electron energy as calculated within the simple HMO scheme is, of course, a rough approximation, but is certainly one of the most reliable outcomes of the HMO model. HMO total π-electron energy was the topic of a number of contemporary investigations[15-17].

The effect ef (G, Z) of a cycle Z on the total π-electron energy of a conjugated system whose molecular graph[13] is G can be calculated from

$$\text{ef}\,(G, Z) = \frac{1}{\pi} \int\limits_{-\infty}^{\infty} \ln \left| \frac{\Phi\,(G, ix)}{\Phi\,(G, ix) + 2\,\Phi\,(G - Z, ix)} \right| dx. \tag{1}$$

In the above formula $i = \sqrt{-1}$ whereas $\Phi\,(G, x)$ symbolizes the characteristic polynomial[13] of graph G. A more precize specification of the notation used in eq. (1) is given in Part C of this paper.

The quantity ef (G, Z) is just an estimate of the effect of the cycle Z on the thermodynamic stability of the corresponding conjugated molecule[8]. If ef $(G, Z) > 0$, then cyclic conjugation along the cycle Z increases the stability of the molecule. If ef $(G, Z) < 0$, then the cyclic conjugation along the cycle Z has a destabilizing effect. These effects have been calculated for a great variety of conjugated molecules[8].

The following regularities have been observed[8] for the quantity ef (G, Z):

(a) If the size of the cycle Z is $4m + 2$ (that is, 6 or 10 or 14 or . . .), then ef (G, Z) is positive.

(b) If the size of the cycle Z is $4m$ (that is, 4 or 8 or 12 or . . .), then ef (G, Z) is negative.

Statements (a) and (b) are known as the extended Hückel (4m + 2)-rule. Its precise formulation was possible for the first time by using graph-theoretical reasoning. Rule (b) was later rigorously proved for alternant hydrocarbons[9] while rule (a) holds only for the great majority, but not for all alternant conjugated hydrocarbons[8,9]. In the following we shall see that a significant violation of the Hückel rule occurs in the case of porphin.

In order to avoid any misunderstanding we point out the basic differences between the Hückel (4m + 2)-rule which holds for monocyclic conjugated systems and its extension to polycyclic molecules. The original Hückel rule states that 4m + 2 π-electrons in a monocyclic conjugated molecule form a stable closed shell configuration, contrary to the case of 4m π-electrons, which form a polyradical open shell configuration. This result holds irrespective of the size of the cycle. Hence, in the standard Hückel rule the number of π-electrons rather than the size of the cycle is the stability-determining factor. We note in passing that the Hückel rule for monocyclic systems is a consequence of symmetry and can be deduced by using group-theoretic arguments.

Attempts to extend the Hückel rule to polycyclic systems have a long history. The main obstacle in the case of polycyclic conjugated molecules is that there is no unambiguous and self-evident way of deciding which part of the total stabilization (or destabilization) due to cyclic conjugation comes

from a particular cycle. In addition, symmetry arguments are of no use in polycyclic systems. Graph-theoretical methods enabled one to overcome these difficulties (although the mere fact that four different ef (G, Z)'s have been proposed in the literature shows that some ambiguity still remains). These graph-theoretical techniques for the calculation of the contribution of a particular cycle to the total effect of cyclic conjugation are discussed in some detail in Part C of the present paper.

In the case of polycyclic conjugated molecules it is not possible to speak about the number of π-electrons in a particular cycle, since these electrons belong simultaneously to all cycles. Therefore, in all approaches towards the extension of the Hückel $(4m + 2)$-rule to polycyclic systems, the size of the cycle rather than the (undefined) number of π-electrons is taken into account. Whenever in the present paper we speak about the Hückel rule we mean its extension to polycyclic conjugated molecules and understand that $4m + 2$ refers to the size of the corresponding cycle.

On the Topology of Porphin

The molecules investigated in the present paper are collected in Figure 1. These are porphin (I), the NH-tautomer of porphin (II), the doubly protonated
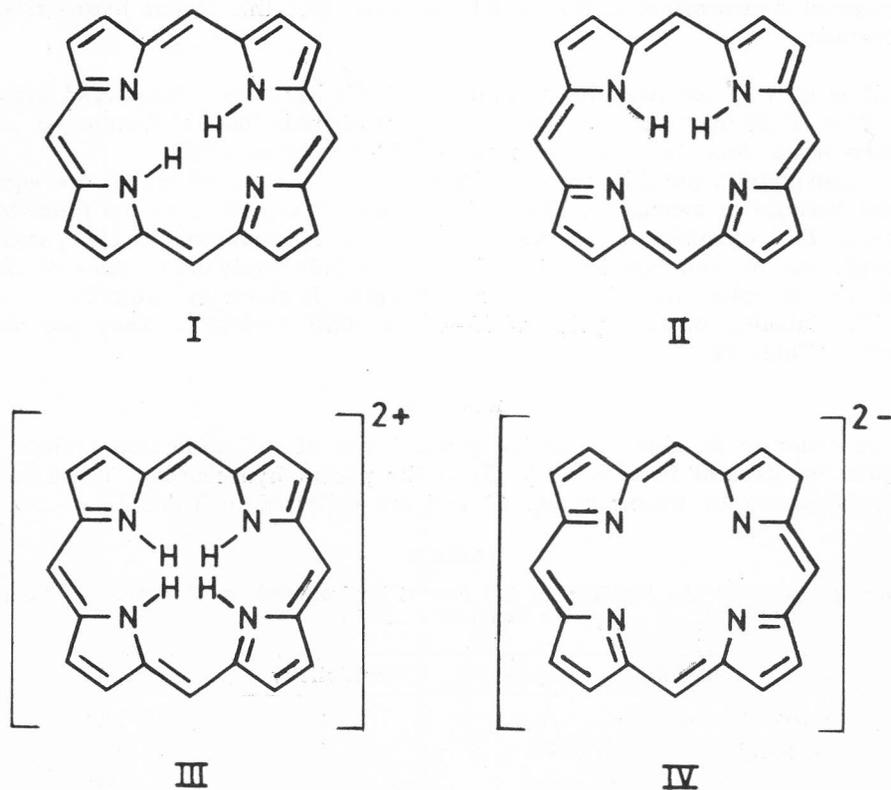
Figure 1. Porphin (I), the NH-tautomer of porphin (II), protonated porphin (III) and deprotonated porphin (IV)

porphin dication (III) and the doubly deprotonated porphin dianion (IV), each having 26 π-electrons.

The topology of the π-electron network of porphin is represented by graph G_P. As a matter of fact, this graph corresponds to a (hypothetical)
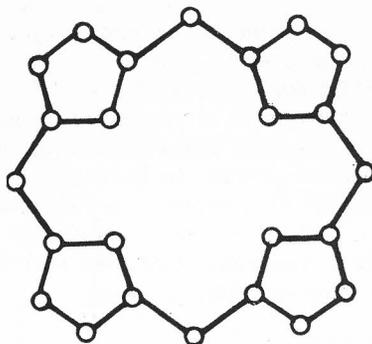
Gp

conjugated hydrocarbon $C_{24}H_{16}$, which we shall call the parent hydrocarbon of porphin.

It is easy to see that the porphin graph G_P has four 5-membered cycles and $2^4 = 16$ distinct macrocycles: one 16-membered, four 17-membered, six 18-membered, four 19-membered and one 20-membered cycle.

Consequetnly, porphin has also 16 macrocycles, some of which are equivalent because of symmetry. They will be labeled according to the following pattern. For example, $Z_{18}(N, NH)$ denotes an 18-membered cycle passing through one N- and one NH-atom. There are four equivalent cycles of this type. The complete list of the cycles of porphin is given in Table II.

The labeling of the cycles of II—IV is fully analogous. They are also listed in Table II.

RESULTS

In order to be able to see the pequliarities of the π-electron system of porphin we present first the ef (G, Z) of the parent hydrocarbon. These have been calculated by means of eq. (1) and are collected in Table I.

TABLE I

Effect of Cycles on the Stability of the Parent Hydrocarbon of Porphin. All Values are in Units of 10^{-6} β

molecule	cycle	multiplicity	ef (G, Z)
parent hydrocarbon	Z_{16}	1	—7522
of porphin	Z_{17}	4	5143
	Z_{18}	6	210
	Z_{19}	4	—193
	Z_{20}	1	—28

An inspection of Table I shows that the Hückel $(4m + 2)$-rule is fully obeyed. Hence, the parent hydrocarbon of porphin behaves just like all other conjugated molecules studied previously[8]. The magnitude of the effects of the cycles is very small and, in addition, significantly decreases with the increase of the size of the cycle. For instance, the effect of the 20 membered cycle is more than 250 times smaller than the effect of the 16-cycle.

The effect of cyclic conjugation in the case of I—IV is drastically different, as it can be seen from Table II. The $ef(G, Z)$ values in Table II are also obtained by means of eq. (1), using the parametrization scheme for the heteroatoms, as recently recommended by Van-Catledge[18].

TABLE II

Effect of Cycles on the Stability of Porphin (I) and its three Derivatives (II—IV). All Values are in Units of 10^{-6} β

molecule	cycle	multiplicity	$ef(G, Z)$
I	Z_{16}	1	7519
	Z_{17} (N, NH, N)	2	9972
	Z_{17} (NH, N, NH)	2	3368
	Z_{18} (N, N)	1	12997
	Z_{18} (N, NH)	4	4201
	Z_{18} (NH, NH)	1	1271
	Z_{19} (N)	2	5161
	Z_{19} (NH)	2	1480
	Z_{20}	1	1702
II	Z_{16}	1	7173
	Z_{17} (N, NH, N)	2	9548
	Z_{17} (NH, NH, N)	2	3255
	Z_{18} (N, N)	1	12491
	Z_{18} (N, NH)	4	4073
	Z_{18} (NH, NH)	1	1244
	Z_{19} (N)	2	5026
	Z_{19} (NH)	2	1457
	Z_{20}	1	1688
III	Z_{16}	1	3878
	Z_{17}	4	4743
	Z_{18}	6	5673
	Z_{19}	4	6615
	Z_{20}	1	7451
IV	Z_{16}	1	12725
	Z_{17}	4	6816
	Z_{18}	6	3248
	Z_{19}	4	1335
	Z_{20}	1	451

DISCUSSION

The first thing that one observes in Table II is that all $ef(G, Z)$ values are positive. Hence, in the case of porphin all cycles present in the molecule contribute towards thermodynamic stabilization. Furthermore, the effects are much larger than in the case of the parent hydrocarbon and only very slightly decrease (or even increase) with increasing the size of the cycle. This all points to an extraordinary stabilization due to cyclic conjugation which

occurs in porphin and which much resembles the conjugation effects in aromatic benzenoid hydrocarbons.

The Hückel $(4m + 2)$-rule is completely violated in porphin. Not only that 16- and 20-membered cycles stabilize the molecule, but odd-membered cycles have comparable or even higher effects.

We may conclude that the above topological analysis revealed the unusual position of the porphin system among conjugated molecules. Its exceptional conjugation pattern may provide a clue for the understanding why Nature has chosen porphyrins to act in the most important biochemical processes.

Some further observations are also worth mentioning.

There has been a long dispute concerning the correct position of the NH hydrogen atoms in porphin[1,2,4]. Cycles of the same type have similar effects in both I and II, but the effects in II are always slightly weaker. Thus, from the viewpoint of cyclic conjugation, the structure I should be somewhat more favourable then the structure II.

Another discussion was about the cycle along which π-electron delocalization occurs in porphin[1,2,4]. The two major candidates were $Z_{18}(N,N)$ and Z_{16}. Our calculation shows that the former is somewhat better, but indicates a third delocalization mode, namely via the two $Z_{17}(N, NH, N)$ cycles (see Figure 2). However, a correct interpretation of our results is that delocali-
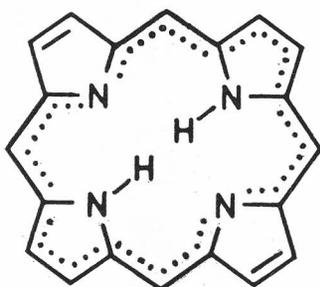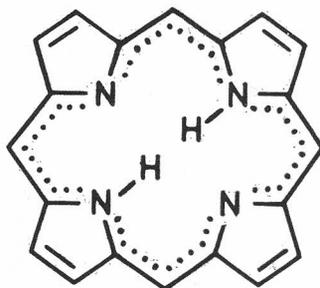
$$Z_{18}(N,N)-\text{model} \qquad Z_{16}-\text{model}$$
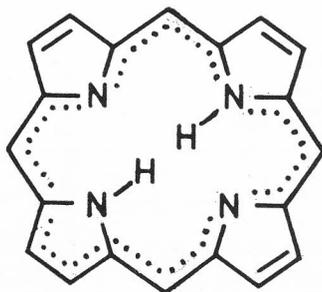
$$Z_{17}(N, NH, N)-\text{model}$$

Figure 2. Delocalization modes in porphin

zation occurs along several cycles simultaneously and that in the case of porphin, the most important among them are Z_{18} (N, N), the two Z_{17} (N, NH, N)'s and Z_{16} (in that order).

PART B

COMMENT ON THE APPLICATION OF THE TOPOLOGICAL RESONANCE ENERGY

METHOD TO PORPHIN

A few years ago the topological resonance energy (TRE) method[19,20] was applied to porphin and some related compounds[21]. In the meantime it became clear that TRE has a number of serious and inevitable shortcomings[22-27]. The paper[21] can be viewed as a typical example of inconclusive and incorrect results reached by the TRE method.

It has been shown[28] that TRE measures the joint effect of all cycles on total π-electron energy. In the case of porphyrins the dominant part of TRE comes from the individual and collective effects of the four pyrrole rings. (We calculated that these contributions are two orders of magnitude greater than the effects of macrocycles examined in Part A of this paper). Therefore, it is not at all surprising that the TRE method cannot account for the much more subtle (and chemically more important) conjugation effects of the large cycles in porphin.

In particular, it has been found[21] that for porphin I, TRE = 0.392 whereas for its open-chain analogue V, TRE = 0.447.

$\underline{\mathbf{V}}$
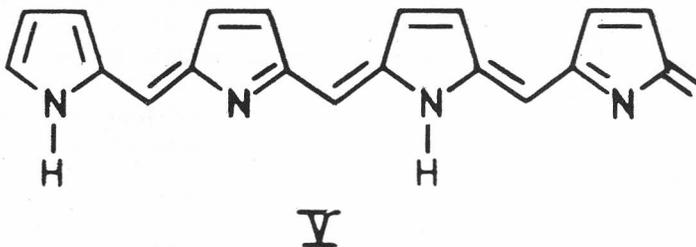
Therefore, the TRE model forces one to conclude that the transformation V → I, which introduces conjugation along the 16-, 17-, 18-, 19- and 20-membered cycles, will substantially decrease the stability of the π-electron system. This absurd conclusion is in obvious contradiction with the entire chemistry of porphyrins and, in particular, with the results obtained in Part A of this paper.

In order to get some information about cyclic conjugation in porphin, the TRE values of its individual cycles have been calculated.[21] This is a further artifact in ref. 21, since it is a rather naive assumption that cyclic conjugation in an isolated cycle is the same as the conjugation along a cycle within a complicated polycyclic molecular topology. The estimates obtained in ref. 21 are, of course, in substantial disagreement (often even in sign) with what is reported in the present paper. It is worth noting that methods for the calculation of ef (G, Z) became available[7,8,29] much before the investigations reported in ref. 21 were completed.

PART C
ON METHODS FOR THE CALCULATION OF THE EFFECT OF CYCLIC CONJUGATION

Four methods for the calculation of the effect of a cycle on total π-electron energy have been proposed[7,10,12,29]. We show now that they are closely related, both formally and numerically. In order to do this we shall use the recently developed μ-polynomial formalism[10].

Let G be a molecular graph[13] and $Z_1, Z_2, \ldots, Z_r$ the cycles contained in it. (For an example see Part A and the discussion concerning the cycles of the porphin graph G_P. For this graph, $r = 20$). Associate a variable weight t_a to each of the cycles Z_a, $a = 1, 2, \ldots, r$, and denote the vector $(t_1, t_2, \ldots, t_r)$ by t.

If $t_1 = t_2 = \ldots = t_r = 0$, then we write $t = 0$. If $t_1 = t_2 = \ldots = t_r = 1$, then we write $t = 1$.

Let $G - Z_a$ be the subgraph of G, obtained by deletion of all vertices of Z_a. Then the μ-polynomial of G is determined by[10]

$$\mu(G, t, x) = \Phi(G, x) + 2 \sum_a (1 - t_a)\, \Phi(G - Z_a, x) +$$

$$+ 2^2 \sum_{a<b} (1 - t_a)(1 - t_b)\, \Phi(G - Z_a - Z_b, x) +$$

$$+ 2^3 \sum_{a<b<c} (1 - t_a)(1 - t_b)(1 - t_c)\, \Phi(G - Z_a - Z_b - Z_c, x) + \ldots \qquad (2)$$

where $\Phi(H, x)$ denotes the characteristic polynomial[13] of the graph H, $H = G$, $G - Z_a$, $G - Z_a - Z_b$ etc. In formula (2) we adopt the conventions that $\Phi(H - Z_i - Z_j, x) = 0$ if Z_i and Z_j are not disjoint (i. e. have common vertices) and that $\Phi(H - Z_i, x) = 1$ if the cycle Z_i embraces all the vertices of H.

Note that if $t = 1$, then the μ-polynomial reduces to the characteristic polynomial.

Define, finally, the unit vectors $e_1, e_2, \ldots, e_r$, such that all components of e_j are zero, except the j-th component which is equal to one, $j = 1, 2, \ldots, r$. Then, of course,

$$t = t_1 e_1 + t_2 e_2 + \ldots + t_r e_r.$$

The HMO total π-electron energy $E(G)$ corresponding to the molecular graph G can be calculated from the characteristic polynomial $\Phi(G)$ according to a well established procedure. This is symbolized by the mapping f

$$f: \ \Phi(G, x) \to E(G).$$

Applying now the same mapping to the μ-polynomial we get a quantity $E(G, t)$

$$f: \ \mu(G, t, x) \to E(G, t)$$

which, of course, depends on the vector t. For $t = 1$, $E(G, t)$ coincides with $E(G)$.

Varying the weight of the cycles of G we formally change the extent to which these cycles contribute to the total π-electron energy. In particular, the choice $t_a = 0$ corresponds to a complete neglect of the effect of the cycle Z_a.

Then the first method[7] for the calculation of the effect of Z_a on $E(G)$ can be formulated as

$$ef_1(G, Z_a) = E(G, 1) - E(G, 1 - e_a) \qquad (3)$$

the method of Aihara[29] reads

$$ef_2 (G, Z_a) = E (G, e_a) - E (G, 0) \tag{4}$$

whereas the recently proposed »local« method[12] obeys

$$ef_3 (G, Z_c) = \partial E (G, t)/\partial t_a \big|_{t=1}. \tag{5}$$

The method proposed in ref. 10. is based on the decomposition of the effect of a cycle Z_a into first-, second-, third- and higher-order contributions. The k-th order contribution coming from the cycle Z_a is given by

$$ef_4^{(k)} (G, Z_a) = (1/k!) \, \partial^k E (G, t)/(\partial t_a)^k \big|_{t=0} \tag{6}$$

and the total effect of Z_a is then

$$ef_4 (G, Z_a) = ef_4^{(1)} (G, Z_a) + ef_4^{(2)} (G, Z_a) + ef_4^{(3)} (G, Z_a) + \ldots \tag{7}$$

In the case of conjugated systems with occupied bonding MO's and empty antibonding MO's, it can be shown[11] that formula (3) reduces to the previously given formula (1). In some exceptional cases, a strict application of (3) would give complex-valued results[30]. This difficulty has been recently overcome[12] by introducing $ef_3 (G, Z_a)$. Nevertheless, in normal situations the use of $ef_1 (G, Z_a)$ and its special form $ef (G, Z_a)$ should be recommended.

We now show that the method proposed in ref. 10 is equivalent to that earlier given by Aihara:

$$ef_2 (G, Z_a) = ef_4 (G, Z_a). \tag{8}$$

In order to do this expand $E (G, \lambda e_a)$ in a power series of λ and assume (as it has already been done in (7)) that the series converges for $\lambda \leq 1$. Direct calculation and the use of (6) give

$$E (G, \lambda \, e_a) = E (G, 0) + ef_4^{(1)} (G, Z_a) \, \lambda + ef_4^{(2)} (G, Z_a) \, \lambda^2 + \ldots$$

Setting $\lambda = 1$ and having in mind (7) we obtain (8).

The three different methods (3), (4) and (5) give, however, very close numerical results, especially in the absence of degenerate and almost degenerate energy levels. We shall demonstrate this fact.

Suppose that the effects of cyclic conjugation on total π-electron energy are nearly additive functions, i. e. that

$$E (G, t) = E (G, 0) + t_1 \, ef^* (G, Z_1) + t_2 \, ef^* (G, Z_2) + \ldots + t_r \, ef^* (G, Z_r) \tag{9}$$

holds at least as a rough approximation. The nature of the coefficients $ef^* (G, Z_a)$ will become clear later on.

Setting $t = 1$ and $t = 1 - e_a$ into (9) and substracting the so obtained equations we arrive at

$$ef_1 (G, Z_a) \approx ef^* (G, Z_a).$$

Setting $t = e_a$ into (9) and having in mind (4) we obtain

$$ef_2 (G, Z_a) \approx ef^* (G, Z_a).$$

Differentiating (9) with respect to t_a and using (5) we get

$$ef_3 (G, Z_a) \approx ef^* (G, Z_a).$$

It is obvious that the approximation (9) becomes an exact formula if the components t_a of t approach zero. Differentiating (9) with respect to t_a and using (6) we see that

$$ef^* (G, Z_a) = ef_4^{(1)} (G, Z_a).$$

This latter relation is an exact one. It shows that the three methods for the estimation of the effect of cyclic conjugation give identical results within the first order (linear) approximation. Differences between $ef_1 (G, Z)$, $ef_2 (G, Z)$ and $ef_3 (G, Z)$ are consequences of second- and higher-order terms which are usually small. This explains why $ef_1 (G, Z)$, $ef_2 (G, Z)$ and $ef_3 (G, Z)$ often have almost identical numerical values.

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SAŽETAK

Ciklička konjugacija u porfinu

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Rad se sastoji od tri dijela. U dijelu A su izložena istraživanja o cikličkoj konjugaciji u porfinu i nekim srodnim spojevima. Pokazano je da je u porfinu narušeno Hückelovo pravilo 4m+2 i to tako da konjugacija uzduž bilo kojeg od 16-, 17-, 18-, 19 i 20-članog prstena uvijek dovodi do stabilizacije π-elektronskog sustava. U dijelu B se daju neke primjedbe na metodu topološke rezonancijske energije i njezinu primjenu na porfin. U dijelu C su uspoređene četiri postojeće metode za procjenu utjecaja cikličke konjugacije na stabilnost π-elektronskih sustava i ukazano je na njihovu međusobnu povezanost.