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QTAIM *N*-Center Delocalization Indices As Descriptors of Aromaticity in Mono and Poly Heterocycles

MARCOS MANDADO, MARÍA J. GONZÁLEZ-MOA, RICARDO A. MOSQUERA
Departamento de Química Física, Facultade de Química, Universidade de Vigo, 36310 Vigo, Galicia, Spain

Received 9 March 2006; Revised 17 April 2006; Accepted 18 April 2006

DOI 10.1002/jcc.20468

Published online 24 October 2006 in Wiley InterScience (www.interscience.wiley.com).

Abstract: The implementation of the *n*-center electron delocalization indices, *n*-DIs, and *n*-order electron localization indices, *n*-LIs, within the framework of the quantum theory of atoms in molecules, QTAIM, is performed. *n*-DIs are shown to be very useful to study the local aromaticity in monocyclic and polycyclic compounds. Total and π *n*-DIs from *n* = 4 to 7 were computed for a series of typical 4, 5, 6, and 7-center aromatic and antiaromatic rings. For *n* \geq 5 the π *n*-DI accounts for the 95% of the total *n*-DI and can be employed alone to measure the aromaticity. A scaling factor on the *n*-DIs is required in order to compare the aromaticity of [5c-6e] and [6c-6e] rings, the same correction allows to estimate the relative aromatic stabilization of polycyclic compounds using the sum of its values for individual rings. This is called Effective Scaled Electron Delocalization, ESED. The comparison with other aromaticity indices reflects a good correlation between ESED and both resonance energies, and HOMA indices. The most important differences between scaled π *n*-DIs and NICS(0) indices are found for compounds that contain rings with different number of centers or π electrons.

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Key words: atoms in molecules; *n*-center delocalization indices; aromaticity; cyclic compounds

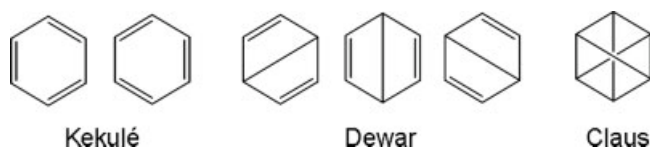
Introduction

Aromaticity is known to be one of the most important features governing the stability and reactivity of unsaturated cyclic and polycyclic compounds. Although no precise, quantitative and generally accepted definition has been given for the aromaticity, it provides the unsaturated ring systems with an extra stabilization that is reflected in a low reactivity compared with nonaromatic ring systems. It is well-known that aromaticity is strongly related to the electron delocalization of the π -electrons along all the centers of the ring. For instance, in benzene, the most significant example of aromatic compounds, several delocalized electronic structures stabilizing the π -electron system were proposed in the chemical literature, those proposed by Kekulé and Leibigs,^{1–3} Dewar,⁴ and Claus⁵ (Scheme 1) being the most well known. However, there are many more resonance structures for benzene (vide infra).

Several indices of aromaticity have been proposed throughout the literature, most of them belonging to two groups: structure based indices and magnetic based indices. All of them were completely reviewed in a recent special issue of *Chemical Reviews*.⁶ Maybe, the most widely structure-based index is the HOMA (harmonic oscillator model of aromaticity) index,^{7,8} based on geometry considerations and calculated by expression,

(1) where *b* is the number of bonds considered and α is an empirical constant fixed to give a value of HOMA = 0 for a non-aromatic model system and HOMA = 1 for a fully aromatic system (a system with all the bonds equal to an optimal value R_{opt}). R_i is the experimental or computed bond lengths. On the other hand, the most widely used magnetic-based index is the NICS (nucleus-independent chemical shift) index,⁹ which is defined as the negative value of the shielding, computed at a ring center (NICS(0)) or at some other interesting point of the system. For aromatic rings, the large delocalization of the π electrons produces a large value for the magnetization at the center of the ring, and the larger the delocalization is, the larger the magnetization will be. In any case, the structure-based and magnetic-based indices predict different aromaticity, unless the molecules compared are closely structurally related.^{10,11} Another way of measuring aromaticity is the calculation of the resonance energy,¹² RE. They are recognized to be the cornerstone of aromaticity, as they are the clearest representation of aromatic stabilization. However, in many cases their calculation is very difficult to evaluate unambiguously, and comparisons to REs values should be done with values obtained using the same method.¹²

Correspondence to: R. A. Mosquera; E-mail: mosquera@uvigo.es



Scheme 1.

$$\text{HOMA} = 1 - \frac{\alpha}{b} \sum_{i=1}^n (R_{\text{opt}} - R_i)^2. \quad (1)$$

In this work, we are concerned with those indices based on electron delocalization measures,¹³ since they are strictly related to the original idea of aromaticity. Poater et al. proposed the average of the two-center electron delocalization indices, DIs, of atoms in para disposition (PDI) as a measure of aromaticity.¹⁴ Although the calculation of PDI indices for several aromatic compounds were proved to be in good concordance with the aromaticity and in some cases with other aromaticity indices as HOMA or NICS,^{14–16} PDI indices are limited to the calculation on 6-center rings and focus too much on Dewar and Claus bonding structures. The same authors have introduced the aromatic fluctuation index, FLU,¹⁷ which is also based on the electron delocalization indices between pairs of adjacent atoms. Also referred to two-center electron delocalization is the bond order index of aromaticity, BOIA, introduced by Bultnick et al.¹⁸ Matta and Hernández-Trujillo^{19,20} reformulated the HOMA aromaticity index in terms of two-center electron delocalization, taking benzene as reference value.

The use of multicenter bond indices as a measure of aromaticity in 5 and 6-center rings was initially proposed by Giambiagi and coworkers.^{21–24} These indices measure the extension of the electron delocalization to all centers of the ring,* which is expected to be especially large for aromatic systems. Moreover, using Mulliken type calculations they showed that different terms involving all the atoms of the ring can be obtained depending on the way followed to calculate the electron delocalization.^{23,24} These terms account for all the delocalized electronic structures, including among them those originally proposed by Kekulé, Dewar, and Claus were shown in Scheme 1.

Recently, Bultnick et al. employed the multicenter bond indices computed from Mulliken type calculations as a measure of local aromaticity in polycyclic aromatic hydrocarbons¹⁸ and homoaromaticity.²⁶ They based their study on the Clar's original idea²⁷ that individual benzenoid rings can be considered as local benzene-like regions, and proposed to characterize the aromati-

city of these rings by the similarity to benzene itself. At the time of writing this paper, we have known that the same authors have extended some of their calculations on polyacenes^{28,29} using the methodology of the Quantum Theory of Atoms in Molecules (QTAIM).^{30,31} The present paper differs from theirs since we study local aromaticity in cycles with diverse number of centers that may contain heteroatoms. Moreover, we propose corrections on the local aromaticity indices to account for total aromaticity in polycyclic compounds, which are compared with REs, HOMA and NICS(0) indices.

In this work, *n*-center delocalization indices, *n*-DIs, are computed on several 4, 5, 6, and 7-center rings within the framework of the QTAIM. We show that the *n*-DIs calculated for QTAIM atoms are not only in good concordance with the aromatic or antiaromatic character, but they also predict the enforcement of the aromaticity for antiaromatic rings when they are linked to aromatic ones. Our goal is to obtain a procedure to compare aromaticities among aromatic compounds whose structures are significantly different, including cyclic and polycyclic compounds, which differ both in the number of centers, *n*, and/or in the number of π electrons, *a*, of the [*nc-ae*] ring, and contain (or not) heteroatoms.

Theoretical Background: Definition of *n*-DIs and *n*-LIs

In order to reach a general definition of *n*-DIs and *n*-order electron localization indices, *n*-LIs, we will start describing the equations for the second-order and third-order cases. The generalization for the *n*-center case will be done afterwards. All the expressions presented in this section are strictly valid for mono-determinant wave functions, the MOs employed can be HF or Kohn-Sham (KS). Nevertheless, it has to be noticed that, for KS formalism, the mono-determinant wave function is an approximation to the real one. Therefore the equations derived below, eqs. (2)–(13), are approximations to the correct DFT indices.³²

Using the diagonal terms of the first-order spin free density matrix, the number of electrons, *N*, can be written in terms of the occupied spatial molecular orbitals as in eq. 2. Partitioning the molecule into QTAIM atomic regions, one can obtain the atomic electron populations with eq. (3), where $\langle ili \rangle_A$ represents the overlap integral within the atomic domain of the atom A.

$$N = 2 \sum_{i=1}^{N/2} \langle ii \rangle^2 \quad (2)$$

$$N_A = 2 \sum_{i=1}^{N/2} \langle ii \rangle_A^2. \quad (3)$$

N can be also written in terms of *n*-order spin-free density matrices. Using the second-order matrix, two different magnitudes, $\delta_2(A, B)$ and $\lambda_2(A)$, are obtained from the expansion of *N*. $\delta_2(A, B)$ is called “two-center electron delocalization index”³³ and measures the electron population shared by atoms A and B. On the other hand, $\lambda_2(A)$ is called “electron localization index”³³ and has been said to represent the nonshared electron population of the atom A.

*These indices measure the extent to which electrons are delocalized or shared over several atomic basins with regard to a zero Fermi hole density. Therefore, there can be specific cases where they can present negative values, as those obtained for several 3c-4e systems (see ref. 25 with values computed with QTAIM). In Hartree-Fock theory this means that the integration of the *n*-electron density function over the basins considered provides a higher probability than that corresponding to consider Coulomb repulsions exclusively.

$$\begin{aligned}
 N &= 2 \sum_{i,j}^{N/2} \langle i|j \rangle \langle j|i \rangle = 2 \sum_{i,j}^{N/2} \sum_A \langle i|j \rangle_A \sum_B \langle j|i \rangle_B \\
 &= 2 \sum_A \sum_B \sum_{i,j}^{N/2} \langle i|j \rangle_A \langle j|i \rangle_B \\
 &= 2 \sum_A \sum_{i,j}^{N/2} \langle i|j \rangle_A \langle j|i \rangle_A + 4 \sum_{B>A} \sum_{i,j}^{N/2} \langle i|j \rangle_A \langle j|i \rangle_B \quad (4)
 \end{aligned}$$

$$\delta_2(A,B) = 4 \sum_{i,j}^{N/2} \langle i|j \rangle_A \langle j|i \rangle_B \quad (5)$$

$$\lambda_2(A) = 2 \sum_{i,j}^{N/2} \langle i|j \rangle_A \langle j|i \rangle_A. \quad (6)$$

It must be mentioned that $\delta_2(A,B)$ has been called “covalent bond order” and the summation of $\delta_2(A,B)$ for an atom A, the “covalent valence index.”³⁴ Nevertheless, $\delta_2(A,B)$ and $\lambda_2(A)$ only represent unequivocally the “covalent bond order” and the “nonshared electron population” in diatomic molecules. In Bader’s view, atoms bonded to A or B may have an important effect on the $\delta_2(A,B)$ values, because of the delocalization of their electron densities into the basins of A or B.³⁵ $\delta_2(A,B)$ values are then invariably somewhat less than the formal bond multiplicity. This fact is expected to be very significant for highly delocalized electronic systems, where the electron delocalization between nonbonded atoms is also important. However, when the presence of a symmetry plane allows to perform a σ/π partitioning, the π electron delocalization index, $\delta_2^\pi(A, B)$,^{36–38} can be unequivocally compared to the “ π -bond order” as long as no π -electrons are shared with other atoms linked to them (for example in ethene). In addition, for molecules with more than two atoms, the value of the “covalent valence index” is overestimated by the summation of the $\delta_2(A,B)$, and $\lambda_2(A)$ does not represent strictly the non-shared electron population for polyatomic molecules (as it will be discussed at the end of this section). Therefore, in what follows, we use “ n -center electron delocalization index” instead of “ n -center covalent bond order” and include a subscript for the electron localization, $\lambda_n(A)$, and electron delocalization, $\delta_n(A,B)$ indices, indicating the matrix-order employed to expand N. In any case, for acyclic and localized electronic systems, $\delta_2(A,B)$ and $\lambda_2(A)$ are expected to be a very good approximation to the “covalent bond order” and the “nonshared electron population,” respectively.

The use of higher order density matrices in Generalized Population Analysis (GPA), was first introduced by Ponec and Uhlik.³⁹ When N is expanded in terms of the third-order spin free density matrix [eqs. (7–10)], three kinds of terms are obtained: $\delta_3(A,B,C)$, the 3-center delocalization index, that represents the extension of electron delocalization between the atoms A, B and C (this is the “three-center covalent bond order” for triatomic molecules); $\lambda_3(A)$, the third-order electron localization index; and $\delta_3(A,B)$, that contains the contributions to the electron delocalization involving A and B. The meaning of these terms was analyzed by Boicchio et al.⁴⁰ and more recently, the same authors calculated 3-center delocalization indices using QTAIM^{41,42} and Becke⁴³ atomic partitionings.

$$\begin{aligned}
 N &= 2 \sum_{i,j,k}^{N/2} \langle i|j \rangle \langle j|k \rangle \langle k|i \rangle = 2 \sum_{i,j,k}^{N/2} \sum_A \langle i|j \rangle_A \sum_B \langle j|k \rangle_B \sum_C \langle k|i \rangle_C \\
 &= 2 \sum_A \sum_{i,j,k}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_A \langle k|i \rangle_A + 6 \sum_{B \neq A} \sum_{i,j,k}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_B \langle k|i \rangle_B \\
 &\quad + 12 \sum_{C>B>A} \sum_{i,j,k}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_B \langle k|i \rangle_C \quad (7)
 \end{aligned}$$

$$\delta_3(A,B,C) = 12 \sum_{i,j,k}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_B \langle k|i \rangle_C \quad (8)$$

$$\lambda_3(A) = 2 \sum_{i,j,k}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_A \langle k|i \rangle_A \quad (9)$$

$$\delta_3(A,B) = 6 \left[\sum_{i,j,k}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_B \langle k|i \rangle_B + \sum_{i,j,k}^{N/2} \langle i|j \rangle_B \langle j|k \rangle_A \langle k|i \rangle_A \right]. \quad (10)$$

Expanding N in terms of the n -order spin free density matrix, the expressions (11)–(13) for the n -center electron delocalization and n -order electron localization are obtained. $\Delta_n(A,B,\dots,M)$ represents the total electron delocalization for n -centers, that is, the total shared-electron population among those n atoms. It is defined as the summation running over those permutations (denoted by P) of the n atoms A, B, ..., M that provide different values of $\delta_n(A,B,\dots,M)$, as defined by eq. (12). The summation in $\delta_n(A,B,\dots,M)$ is the “ n -center electron delocalization term” assigned to every specific permutation.^{23,24} The multiplying constant $4n$ in eq. (12) includes a factor 2 due to spin and $2n$ accounting for the number of permutations that are always equivalent, even in a cycle of C1 symmetry (n because of the possibilities to select the starting atom and 2 for clockwise and anticlockwise). Permutations of the atoms in eq. (12) provide different values when $n > 3$. This fact was first observed by Giambiagi et al.^{23,24} and employed to estimate the electron delocalization due to Kekulé, Dewar and Claus delocalized structures in the benzene ring by the calculation of Mulliken type 6-center delocalization indices. $\lambda_n(A)$, is the n -order electron localization index.

$$\Delta_n(A,B,\dots,M) = \sum_P \delta_n(A,B,\dots,M) \quad (11)$$

$$\delta_n(A,B,\dots,M) = 4n \sum_{i,j,k,\dots,m}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_B \cdots \langle m|i \rangle_M \quad (12)$$

$$\lambda_n(A) = 2 \sum_{i,j,k,\dots,m}^{N/2} \langle i|j \rangle_A \langle j|k \rangle_A \cdots \langle m|i \rangle_A. \quad (13)$$

The splitting of n -DIs and n -LIs into σ and π contributions can be done, when allowed by symmetry, as previously performed for 2-center delocalization indices,^{36–38} restricting the summations in eqs. (12) and (13) to π or σ MOs.

To finish this section, we remark that $\Delta_n(A,B,\dots,M)$ only represents the n -center bond order when n is the number of

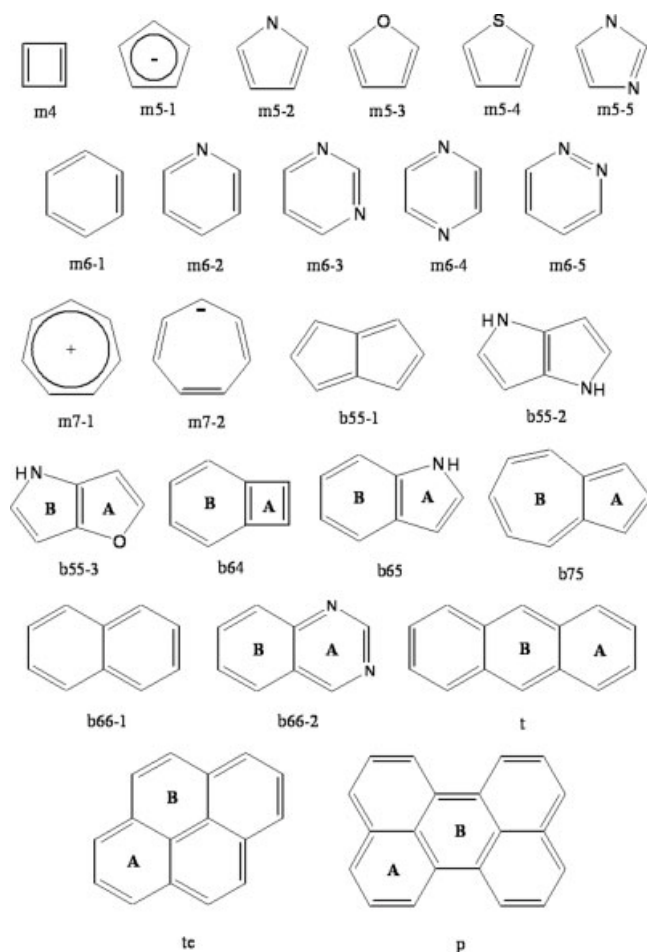


Figure 1. Molecules studied and molecular nomenclature employed.

atoms in the molecule. The π -indices are the exception, since n only comprises, in a good approximation, the atoms belonging to the π system, to obtain the n -center π -bond order, $\Delta_n^\pi(A, B, \dots, M)$. Moreover, a reformulation of the “covalent valence index”³⁴ of an atom A in terms of electron delocalization should be done considering that: the presence of n -DIs with $n > 2$ implies that the summation of the $\delta_2(A, B)$ values for the atom A overestimates its shared electron population. For instance, in triatomic molecules such as H_3^+ , the value of each $\delta_2(H, H)$ is 4/9, resulting in a “covalent valence index” of 8/9, which is larger than the electron population presented by a hydrogen atom in this molecule.

Computational Details

We have chosen molecules containing from 1 to 5 rings, and rings composed by 4, 5, 6 and 7 centers, some of them incorporating heteroatoms in their structures. The set of molecules studied is summarized in Figure 1, together with the nomenclature employed throughout the work. This nomenclature consists in a small letter indicating when the molecule is monocyclic (m) or bicyclic (b) followed by a series of numbers indicating the num-

ber of centers of each ring. Another number, separated by a dash, is added at the end in order to differentiate compounds that present the same number of rings and centers, but different atoms or different atomic disposition. The series is completed with three polycycles of 6-center rings, anthracene (t), pyrene (te) and perylene (p).

The calculations were carried out on Kohn-Shan MOs computed at the B3LYP/6-311++G(d,p) level of calculation. The Gaussian 03 program⁴⁴ was employed to obtain both the molecular structures and the MOs. The AIM-PAC package of programs developed by Bader et al.⁴⁵ was used to integrate the Atomic Overlap Matrix (AOM) within the atomic domains. We have developed a program written in Fortran language to compute the n -DIs and the n -LIs according to eqs. (11)–(13) from $n = 2$ to $n = 8$.⁴⁶ The program computes only $\delta_n(A, B, \dots, M)$ values for every nonequivalent delocalization and considers the number of equivalent permutations for a certain set of atoms. It has to be stressed that computation of n -DIs for $n > 8$ is extremely time consuming.

We have computed the total n -DIs for a few molecules, but only the π - n -DIs are presented in this work. We have confirmed that when $n \geq 5$ the π - n -DI corresponds to 95% of the total n -DI for the molecules here studied. In fact, high-order electron delocalization is expected to be significant only for π -electrons. The use of π -MOs instead of all MOs reduces considerably the computational cost. As pointed out by Bultinck et al.²⁸ for their calculations of multicenter delocalization indices, all the terms from the AOM are employed. So, the accuracy of the QTAIM numerical integration must be checked not only by means of the L integration function³⁰ and the summation of the atomic populations, but also by checking the nondiagonal terms from the AOM. Bultinck et al. checked the accuracy of their calculations comparing the summation of the AOM terms for a pair of MO i, j , $\sum_A \langle i|j \rangle_A$, with the value of the overlap integral over the whole space, $\langle i|j \rangle$. We have checked our calculations in the same way as Bultinck et al.,²⁸ finding differences between $\langle i|j \rangle$ and $\sum_A \langle i|j \rangle_A$ less than 3×10^{-5} for all cases. Moreover, we have checked the accuracy of the calculations performing a different analysis, computing N using terms of the n -order density matrix (including all the terms of the AOM). Thus, N was found to be 27.998, 35.991 and 41.990 for m4, m5-1 and m6-1 using, respectively, terms of the 4, 5 and 6-order density matrices. To reach this level of accuracy, the integrations of the AOMs within the atomic basins were performed with a tight grid.

We have computed NICS(0) and HOMA indices for the rings studied using the same computational level. R_{opt} and α parameters employed for calculating HOMA were taken from ref. 47.

Results and Discussion

QTAIM n -DIs As Local Aromaticity Descriptors

The ability of $\Delta_n^\pi(A, B, \dots, M)$ values to account for the local aromaticity has been tested by calculating them (Table 1) for all the rings of compounds shown in Figure 1. The results obtained for 4 to 7 center rings are discussed below separately, comparing the trends displayed by $\Delta_n^\pi(A, B, \dots, M)$ values with widely accepted qualitative trends for aromaticity.

Table 1. HOMA, NICS(0), Δ_n^π (A, B, ..., M) and $^S\Delta_n^\pi$ (A, B, ..., M) Values Calculated for the Rings Drawn in Figure 1.

	HOMA	NICS(0)	Δ_n^π	$^S\Delta_n^\pi$
m4	-3.998	21.50	0.0054	0.0056
b64(A)	-1.585	23.67	0.0192	0.0267
m5-1	0.809	-15.00	0.0418	0.0365
m5-2	0.854	-13.62	0.0267	0.0228
m5-3	0.185	-11.88	0.0174	0.0148
m5-4	0.752	-12.87	0.0252	0.0215
m5-5	0.881	-13.10	0.0302	0.0260
b55-1	-0.358	24.83	0.0057	0.0073
b55-2	0.846	-13.72	0.0155	0.0158
b55-3(A)	0.184	-10.86	0.0096	0.0096
b55-3(B)	0.875	-13.83	0.0172	0.0176
b65(A)	0.711	-12.43	0.0133	0.0139
b75(A)	0.304	-17.11	0.0130	0.0159
m6-1	0.988	-8.03	0.0267	0.0275
m6-2	0.995	-6.82	0.0252	0.0258
m6-3	0.999	-5.51	0.0242	0.0246
m6-4	0.996	-5.30	0.0241	0.0245
m6-5	0.981	-5.33	0.0256	0.0261
b66-1	0.783	-8.55	0.0143	0.0176
b66-2(A)	0.871	-6.24	0.0130	0.0154
b66-2(B)	0.822	-8.23	0.0140	0.0176
t(A)	0.629	-7.50	0.0107	0.0132
t(B)	0.720	-11.47	0.0098	0.0149
te(A)	0.853	-11.27	0.0133	0.0187
te(B)	0.573	-3.88	0.0067	0.0112
p(A)	0.773	-5.69	0.0129	0.0182
p(B)	0.016	8.00	0.0021	0.0047
b64(B)	0.672	-0.50	0.0185	0.0225
b65(B)	0.916	-9.69	0.0167	0.0201
m7-1	0.984	-6.21	0.0126	0.0150
m7-2	0.073	-2.42	-0.0006	-0.0005
b75(B)	0.612	-5.63	0.0042	0.0044

The capital letters in parentheses are used to refer the individual rings in polycyclic compounds.

7-Center Rings

The values of Δ_7^π for the series formed by cycloheptatriene cation (m7-1) and anion (m7-2), and ring B of compound b75 support the ability of Δ_n^π (A, B, ..., M) as aromaticity descriptor. Thus, for m7-2, an example of [7c-8e] antiaromatic compound, Δ_7^π is almost zero, whereas for m7-1, an example of [7c-6e] aromatic compound, Δ_7^π displays a noticeable increase of the electron delocalization. As for the b75(B) ring, Δ_7^π is in between of aromatic and antiaromatic values.

6-Center Rings

As expected, benzene (m6-1) shows the highest Δ_6^π value with small differences with regard to nitrogen containing compounds (m6-2 to m6-5). Thus, the inclusion of N atoms decreases Δ_6^π in a very small degree, and even the —N=N— unit included in m6-5 seems to be equivalent to only one N atom (m6-2) in terms of Δ_6^π . In b64 (B), b66-1, b66-2(A), b66-2(B), b65(B), t(A), t(B), te(A), te(B), p(A) and p(B) (the corresponding rings in parenthesis), Δ_6^π displays quite smaller values than those of

the corresponding monocyclic compounds. Moreover, as previously found using Mulliken type calculations,¹⁸ the rings that present a larger number of bridge atoms (ring B in t, te, and p), display smaller Δ_6^π . It can be observed that Δ_6^π of bicyclic systems increases with regard to naphthalene when the benzene ring is fused to cycles that display less π -delocalization. Thus, Δ_6^π for b64(B) and b65(B) are larger than for b66-1, whereas b66-1 and b66-2(B) present very similar values. This can be explained considering that the π electron population of the bridge atoms of a certain ring, R, are more involved in the electron delocalization of this ring when they fuse R to a less delocalized R' ring than when they fuse it to a similar ring. b64 represents an extreme case, where the benzene is fused to an antiaromatic cycle, consequently it shows the largest Δ_6^π value in this series.

5-Center Rings

Within the series of [5c-6e] systems formed by m5-1, m5-2, m5-3, and m5-4 molecules, Δ_5^π values show larger differences than Δ_6^π ones for the [6c-6e] systems. The largest value is displayed by the cyclopentadiene anion (m5-1), whereas furane (m5-3), the ring with the largest electronegative heteroatom, presents the smallest one. For b55-1, b55-2, b55-3(A), b55-3(B), b65(A) and b75(A), Δ_5^π values show trends that parallel the expected aromaticity character of these rings. For instance, according to the Hückel rule, it is expected that the antiaromatic compound b55-1 displays a small extension of π -electron delocalization along the 5 centers. On the contrary, the aromatic compounds b55-2, b55-3, b65, and b75 are expected to delocalize their π -electron charge in a large extent. Finally, it has to be mentioned that Δ_5^π values calculated for pirrol rings fused to other aromatic rings (b55-2, b55-3(B), b65(A)) increases as the aromaticity of the other ring decreases, similarly to that found for Δ_6^π in benzene rings.

4-Center Rings

The values of Δ_4^π for cyclobutadiene (m4) and ring A of b64 are a good example of the ability of Δ_n^π (A, B, ..., M) to account for those reactivity changes related to aromaticity. m4 is probably the most significant example of antiaromatic compound and, as a matter of fact, it shows a very high reactivity as dienophile in Diels–Alder type reactions.⁴⁸ When it fuses to a benzene ring its reactivity lowers and b64 becomes a more selective reactant in Diels–Alder processes.⁴⁸ Thus, an increase of the local aromaticity for b64(A) ring has been called as an explanation for this selectivity.⁴⁸ A reflect of this fact are the values of Δ_4^π for m4 and b64(A), justifying the selectivity of b64 in Diels–Alder reactions.

Comparison between Rings with Different Number of Centers and/or π electrons. Scaled n -DIs

π n -DIs cannot be used as a direct measure of the relative aromaticity of rings with different number of centers, n . The reason is the number of centers is the same as the order of the density matrix employed to calculate the π n -DI value. Thus, there is a decrease of π n -DI values associated to the increase in n , but it is not related to the aromatic stabilization, AS. In other words, a certain 5-membered can display less AS than a 6-membered ring

even when the corresponding 5-DI is larger than the 6-DI. Therefore, an expression for obtaining AS from the π n -DI must correct for such a dependency on n . Moreover, the π n -DI measures the extension of the π electron delocalization along all the centers of the ring, but it does not give any information of how much of the total π electrons, N^π , is shared over these centers, which is a useful variable to be related with AS. Summarizing, AS should be a function of the n -DI, n , and N^π . Unfortunately, the relationship linking AS with n -DI, n , and N^π is unknown. So, we can only suggest equations on a qualitative basis, and check their validity comparing the results provided by them with the values of the AS obtained from other methods, such as the resonance energies.¹²

Thus, eq. (14) is a trying equation for linking AS and n -DIs that takes into account the facts commented above. The unknown factor C is a common constant for rings with different number of centers and π electrons. The value of the π n -DI is divided by N^π in order to introduce the fraction of shared π electrons instead of the total shared π electrons, and the number of centers, n , is a multiplying factor introduced to compensate the n -dependency of the π n -DI in 5- and 6-membered rings. The magnitude shown in eq. (15), $^s\Delta_n^\pi(A, B, \dots, M)$, called the scaled n -DI in what follows, displays a good linear correlation with the REs for [5c-6e] and [6c-6e] aromatic systems (vide infra). However, when the eq. (15) is applied on [4c-4e] antiaromatic systems, it provides larger relative values of AS than those expected, probably due to the AS vs n linear relation, proposed in eq. (14), does not hold for these systems.

$$AS \approx C \frac{n}{\sum_{A=1}^n N^\pi(A)} \Delta_n^\pi(A, B, \dots, M) \quad (14)$$

$$^s\Delta_n^\pi(A, B, \dots, M) = \frac{n}{\sum_{A=1}^n N^\pi(A)} \Delta_n^\pi(A, B, \dots, M). \quad (15)$$

Figure 2 represents the comparison of $\Delta_n^\pi(A, B, \dots, M)$ values for several [6c-6e] and [5c-6e] monocycles with the resonance energies, REs, and the I_A aromaticity indices taken from ref. 49. The latter are based upon a statistical evaluation of the extent of variation of ring bond order.⁵⁰ Thus, in Figure 2 it can be noticed that Δ_5^π and Δ_6^π values are in different scales. However, the replacement of n -DIs by their scaled values leads to an acceptable linear correlation with the REs for [5c-6e] and [6c-6e] systems.

Scaled n -DIs: A Tool to Compare the Aromatic Stabilization of Cyclic and Polycyclic Compounds

Another important drawback arises when comparing the π n -DIs with the AS of polycyclic compounds. Although the effect of fused rings over the electron delocalization of a certain ring is implicit in the $\Delta_n^\pi(A, B, \dots, M)$ values, the extension of the π -electron delocalization due to atoms belonging to different rings is not considered. Therefore, an expression of the total system electron delocalization, TSED, of a polycyclic compound must contain terms including the electron delocalization between individual rings. Thus, terms Δ_{ij}^π and Δ_{ijk}^π , introduced in eq. (16),

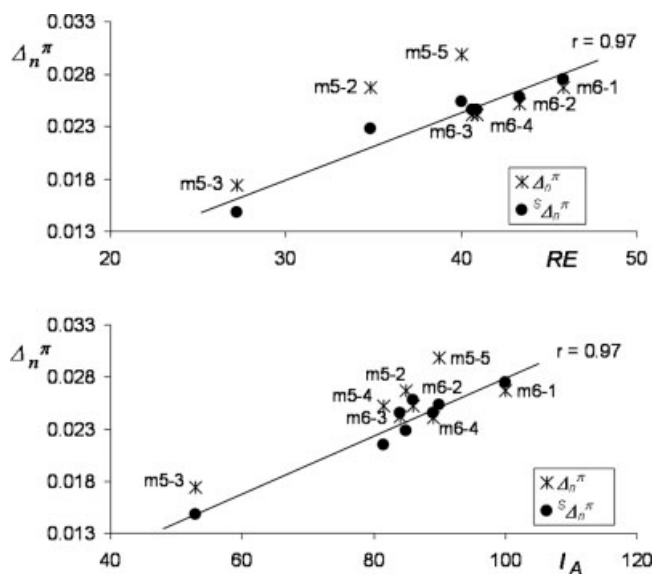


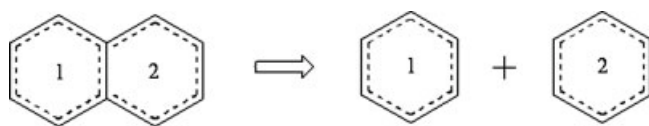
Figure 2. Comparison of $\Delta_n^\pi(A, B, \dots, M)$ and $^s\Delta_n^\pi(A, B, \dots, M)$ with the resonance energies, REs, and I_A indices taken from ref. 49 for some of the [6c-6e] and [5c-6e] monocycles shown in Figure 1.

represent respectively the electron delocalization involving two and three rings. In this equation n_R is the number of rings.

$$TSED = \sum_{i=1}^{n_R} \Delta_n^\pi(A, B, \dots, M)_i + \sum_{i=1}^{n_R-1} \sum_{j>i}^{n_R} \Delta_{ij}^\pi + \sum_{i=1}^{n_R-2} \sum_{j>i}^{n_R-1} \sum_{k>j}^{n_R} \Delta_{ijk}^\pi + \dots \quad (16)$$

On first thoughts, the way to compute terms involving two or more rings could come through the calculation of n -DIs including all the atoms, for instance, the 10-DI for naphthalene. Unfortunately, as commented in the Computational Details section, the calculation of n -DIs using eqs. (11) and (12) with $n > 8$ is very expensive in computational terms. Moreover, the n -DI values for 9 and 10 centers decrease dramatically (9-DI for indole is 4.2×10^{-4} au and 10-DI for naphthalene is 4.0×10^{-4} au) compared to those of 5 and 6 centers (both the 5-DI for pyrrole and the 6-DI for benzene are 2.67×10^{-2} au). So, n -DIs involving two or more rings although reflect the extension of the electron delocalization in a polycycle do not report information, in a practical sense, to account for the relative aromatic stabilization.

Therefore, we propose a simple approximation for estimating the AS in a polycyclic compound by means of the n -DIs of the individual rings. It is initially based on the assumption that the electron delocalization within each ring in a polycycle mainly decreases because part of the electron population of the bridge atoms is also delocalized within the other rings connected by them. The π electron population of a polycycle, N^π , can be partitioned into the ring π electron populations, $N^\pi(r)$, associated to each ring, r , using the atomic π electron populations, $N^\pi(\Omega)$, as indicated by eq. (17). In eq. (17), $f(\Omega)$ represents the number of rings fused by the atom Ω and $n(r)$ is the number of atoms (or



Scheme 2.

centers) of a certain ring r . Thus, we obtain a set of hypothetical non-fused rings (Scheme 2 for naphthalene). Introducing $N^\pi(r)$ given by (17) in definition (14) and summing to all the rings in the polycycle, we get an approach to AS given by eq. (18). Thereby, considering, (15) the calculation of the AS in polycyclic compounds is approximately proportional to the addition of individual ${}^S\Delta_n^\pi(A, B, \dots, M)$ values. Finally, we define the Effective Scaled Electron Delocalization, ESED, given by eq. (19).

$$N^\pi = \sum_{r=1}^{n_R} N^\pi(r) = \sum_{r=1}^{n_R} \sum_{\Omega=1}^{n(r)} \frac{N^\pi(\Omega)}{f(\Omega)} \quad (17)$$

$$\begin{aligned} AS &\approx C \sum_{r=1}^{n_R} \frac{n(r)}{\sum_{\Omega=1}^{n(r)} \frac{N^\pi(\Omega)}{f(\Omega)}} \Delta_n^\pi(A, B, \dots, M)_r \\ &= C \sum_{r=1}^{n_R} {}^S\Delta_n^\pi(A, B, \dots, M)_r \end{aligned} \quad (18)$$

$$\begin{aligned} \text{ESED} &= \sum_{r=1}^{n_R} \frac{n(r)}{\sum_{\Omega=1}^{n(r)} \frac{N^\pi(\Omega)}{f(\Omega)}} \Delta_n^\pi(A, B, \dots, M)_r \\ &= \sum_{r=1}^{n_R} {}^S\Delta_n^\pi(A, B, \dots, M)_r \end{aligned} \quad (19)$$

Table 1 collects the calculated ${}^S\Delta_n^\pi(A, B, \dots, M)$, NICS(0), and HOMA values together with the values of $\Delta_n^\pi(A, B, \dots, M)$ previously commented. It must be remarked that the NICS indices have been shown to be problematic as local aromaticity descriptors for polycyclic compounds in several recent works.^{15,51–55} Moreover, the bond distances between bridge atoms are considered in the calculation of the HOMA indices for the individual rings of a polycyclic compound. These bond distances are part of two rings and thus, depend upon the aromaticity of both rings, as well as the aromaticity due to electron delocalization between rings. All of that makes the HOMA indices problematic to account for the local aromaticity, but the summation of HOMA obtained for each cycle is a good approximation to the total aromaticity in aromatic polycyclic compounds, as shown later on.

The comparison of HOMA and NICS(0) with the $\Delta_n^\pi(A, B, \dots, M)$ and the ${}^S\Delta_n^\pi(A, B, \dots, M)$ values for the individual rings (Table 1) provides some remarkable differences:

- HOMA and NICS(0) values do not predict any attenuation of the antiaromatic character of cyclobutadiene, m4, in benzocyclobutadiene, b64. In fact, the NICS(0) values predict a small increase of the antiaromatic character. Both the Δ_4^π and the ${}^S\Delta_4^\pi$ values increase significantly for b64(A) with regard to m4.

- NICS(0) values are larger for [5c-6e] than [6c-6e] systems. On the contrary, both HOMA and ${}^S\Delta_n^\pi(A, B, \dots, M)$ display larger values for 6-center rings, with the exception of m5-1 for ${}^S\Delta_n^\pi(A, B, \dots, M)$.
- The most aromatic of the [5c-6e] monocyclic systems is the cyclopentadienyl anion (m5-1), except for HOMA values, which are not very convenient to study charged species because the R_{opt} values are obtained from neutral molecules. Moreover, both scaled and unscaled values of n -DIs would indicate that m5-1 is more aromatic than benzene (m6-1). This contradicts the expected sequence of reactivity. About that: on one hand, relative reactivity should not be taken as a comparison of aromaticity, even more when one of the species is charged and the other is neutral. On the other, m5-1 presents larger cyclic conjugation energy than m6-1, according to values calculated by Chesnut and Davis using differential bond separation reactions.⁵⁶ Moreover, pyrrole (m5-2) and furane (m5-3) present smaller cyclic conjugation energy than m6-1,⁵⁶ in line with our results for scaled n -DIs (Table 1). Nevertheless, it has to be noticed that the sequence of cyclic conjugation energies of m5-1 and m6-1 is reversed when this quantity is calculated from homodesmotic reactions in the same paper.⁵⁶
- Although the cycloheptatrienide anion (m7-2) is a well-known example of antiaromatic ring, the NICS(0) value does not reflect it, as in the case of b55-1 or m4. In fact, the NICS(0) value of m7-2 (−2.42) could be considered within the range of weak aromatic compounds. The opposite trend is found for HOMA and Δ_7^π or ${}^S\Delta_7^\pi$ values, which clearly reflects the antiaromatic character of m7-2

It must be notice that the ${}^S\Delta_6^\pi$ values, which incorporate the electron delocalization between fused rings, predict a higher aromaticity for the inner ring than for the outer rings in anthracene, contrary to the Δ_6^π values, and in agreement with the HOMA, FLU,¹⁷ and NICS(0) indices, the study of ring currents of [*n*]acenes,^{57–61} the calculation of resonance energies,^{62–64} and graph theory based descriptors.⁶⁵ The reverse trend is obtained using indices based on molecular quantum similarity,²⁸ Polanski indices,⁶⁶ bond resonance energies and geometry independent electron currents,⁶⁷ and the circuit resonance energies recently calculated by Aihara.⁶⁸ In our point of view, discrepancies between methods are due to the different nature of the corresponding local aromaticity values. Magnetic criteria, such as NICS and ring currents, incorporate electron delocalization that involves more rings when calculating local values. The same is true for the ring resonance energies calculated using the conjugated circuits model. The effects of other rings on local aromaticity computed with HOMA indices were commented above. In contrast, other indices, like unscaled n -DIs, molecular quantum similarity based indices, and circuit resonance energies, are exclusively related to the electron delocalization within a certain ring. Finally, the PDI indices calculated for the rings of anthracene are so similar, that the trend obtained for inner and outer rings depends on the computational level. Thus, values of 0.061 and 0.067 were obtained, respectively, for outer and inner rings at the HF/6-31G**//B3LYP/6-31G*,¹⁴ whereas a common value of 0.066 was obtained at the B3LYP/6-31G**//B3LYP/6-31G*,⁶⁹ and 0.0652 and 0.0649 values were obtained in this work using the B3LYP/6-311++G**//B3LYP/6-311++G** level.

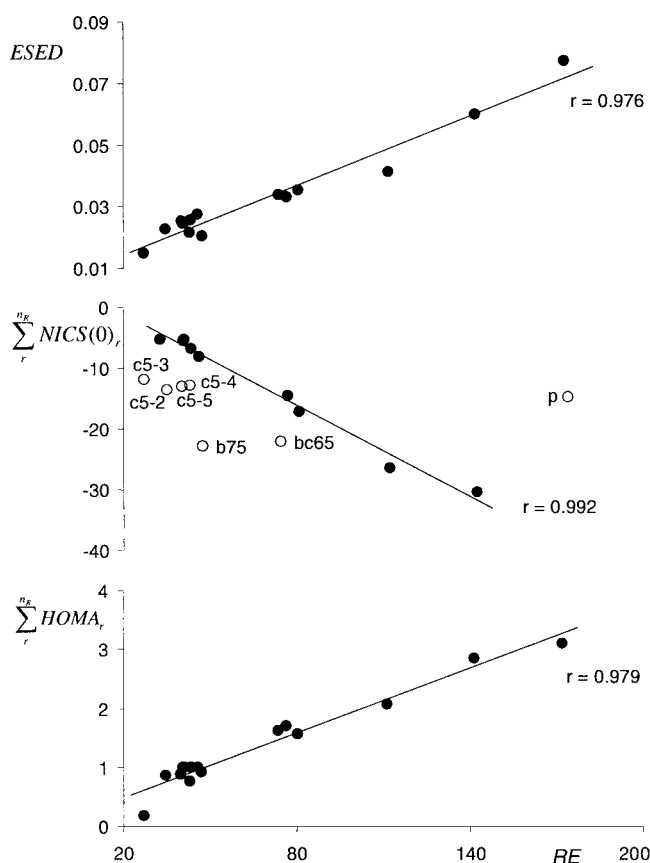


Figure 3. Comparison of ESED, $\sum_{r=1}^{n_R} \text{NICS}(0)_r$, and $\sum_{r=1}^{n_R} \text{HOMA}_r$ values with the resonance energies, REs, taken from ref. 49 for 16 of the monocyclic and polycyclic compounds shown in Figure 1.

Figure 3 displays the correlations found between the REs calculated by Bird⁴⁹ vs. the ESED, $\sum_{r=1}^{n_R} \text{NICS}(0)_r$ and $\sum_{r=1}^{n_R} \text{HOMA}_r$ values, i.e. the summation of the $^S\Delta_n^\pi(A, B, \dots, M)$, NICS(0) and HOMA values for the individual rings, for 16 of the cyclic and polycyclic compounds drawn in Figure 1. ESED and $\sum_{r=1}^{n_R} \text{HOMA}_r$ values show good linear correlations with the REs. However, $\sum_{r=1}^{n_R} \text{NICS}(0)_r$ values only show linear correlation with the REs for cyclic and polycyclic compounds that are composed by 6-center rings, with the exception of perylene (p). $\sum_{r=1}^{n_R} \text{NICS}(0)_r$ values for [6c-6e] and [5c-6e] systems are in different scales, so they cannot be compared. Also, a polycyclic compound as perylene, composed by several benzenoid rings, is out of the line, mainly due to the high antiaromatic character of its inner ring predicted by the NICS(0) value (Table 1). It has to be noticed that the good correlation between ESEDs and REs also holds for a large set of polybenzenoid hydrocarbons that contains from 2 to 7 benzene rings.⁷⁰

Figure 4 displays a comparison of ESED with $\sum_{r=1}^{n_R} \text{HOMA}_r$ and $\sum_{r=1}^{n_R} \text{NICS}(0)_r$. ESED values correlate linearly with $\sum_{r=1}^{n_R} \text{HOMA}_r$ as long as the negative $\sum_{r=1}^{n_R} \text{HOMA}_r$ values are obtained for antiaromatic compounds (m4, b55-1 and b64) are excluded. Charged m5-1 and m7-1 compounds are the worst fitted, probably due to the use of R_{opt} for noncharged systems in the calculation of the HOMA indices. On the other hand, [6c-6e]

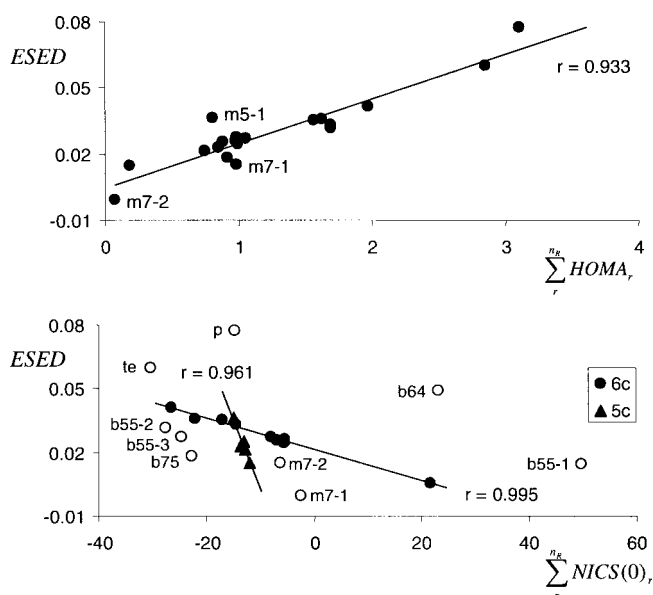


Figure 4. Comparison of $\sum_{r=1}^{n_R} \text{HOMA}_r$ and $\sum_{r=1}^{n_R} \text{NICS}(0)_r$ with the ESED values for the aromatic compounds drawn in Figure 1. Open face circles in $\sum_{r=1}^{n_R} \text{NICS}(0)_r$ vs. ESED plot represent the compounds not included in any of the linear correlations because of clear specific behavior. Outliers in $\sum_{r=1}^{n_R} \text{HOMA}_r$ vs. ESED plot correspond to charged systems.

and [5c-6e] monocyclic systems need to be compared separately in order to find some correlation between ESED and $\sum_{r=1}^{n_R} \text{NICS}(0)_r$, whereas these magnitudes are not correlated for polycycles. However, some of those comprising only 6-center rings (b66-1, b66-2 and t) fit in the same line as [6c-6e] monocyclic systems. It must be also noticed that the m4 antiaromatic compound ([4c-4e] system) fits in the same line as the [6c-6e] systems.

Finally, we have also compared the $\Delta_n^\pi(A, B, \dots, M)$ values with the PDI values for 6-center rings. Figure 5 shows a good correlation between both indices. However, when the values of $\Delta_n^\pi(A, B, \dots, M)$ are replaced by $^S\Delta_n^\pi(A, B, \dots, M)$, a worse correlation is found due to the polycyclic compounds. Notice that

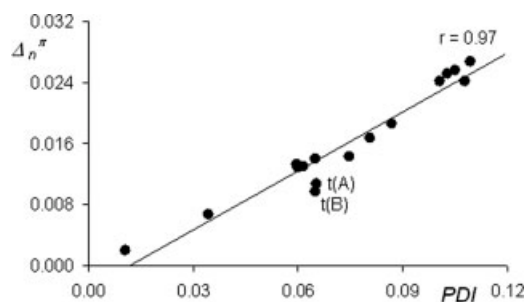


Figure 5. Comparison of $\Delta_n^\pi(A, B, \dots, M)$ with the PDI values for the 6-center rings drawn in Figure 1. Outliers correspond to the rings of anthracene.

the use of PDI indices, for the same reason as the $\Delta_n^\pi(A, B, \dots, M)$ values, is restricted to the study of local aromaticity.

Concluding Remarks

π *n*-DIs are shown to be a useful tool to investigate the local aromaticity in monocyclic and polycyclic compounds. π *n*-DIs can also be employed to study those changes of reactivity related to aromaticity. However, the comparison of aromaticity of [5c-6e] and [6c-6e] rings requires the inclusion of a scaling factor that weights the π *n*-DIs according to the number of centers and π electrons in the ring. The scaled *n*-DIs provide a way to compare the relative aromaticity of polycyclic compounds by summing the individual values of scaled *n*-DIs, once the π electron population of the polycycle has been partitioned into ring populations. The sum defines the effective scaled electron delocalization (ESED).

The good correlation found between REs and ESED values, shows that the latter are, in a good approximation, proportional to the aromatic stabilization in cyclic and polycyclic compounds. On the other hand, [6c-6e] and [5c-6e] monocyclic systems need to be compared separately in order to find some correlation between the ESEDs and $\sum_{r=1}^{nR} \text{NICS}(0)_r$ values, whereas most polycycles do not show any correlation. Nevertheless, some of those comprising only 6-center rings (naphthalene, quinoxaline, and anthracene) fit in the same line as [6c-6e] monocyclic systems. The most important differences between ESED and $\sum_{r=1}^{nR} \text{HOMA}_r$ values are found for charged aromatic compounds.

Acknowledgment

We thank Dr. P. Bultinck for helpful discussions and for providing useful references.

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