

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/6206048>

Multidimensionality of delocalization indices and nucleus independent chemical shifts in polycyclic aromatic hydrocarbons

ARTICLE *in* JOURNAL OF COMPUTATIONAL CHEMISTRY · FEBRUARY 2008

Impact Factor: 3.59 · DOI: 10.1002/jcc.20794 · Source: PubMed

CITATIONS

48

READS

8

3 AUTHORS, INCLUDING:



Stijn Fias

Vrije Universiteit Brussel

31 PUBLICATIONS 624 CITATIONS

SEE PROFILE

Multidimensionality of Delocalization Indices and Nucleus Independent Chemical Shifts in Polycyclic Aromatic Hydrocarbons

STIJN FIAS, SOFIE VAN DAMME, PATRICK BULTINCK

Department of Inorganic and Physical Chemistry, Ghent University, Krijgslaan 281 (S3),
9000 Gent, Belgium

Received 2 April 2007; Revised 21 May 2007; Accepted 22 May 2007

DOI 10.1002/jcc.20794

Published online 13 July 2007 in Wiley InterScience (www.interscience.wiley.com).

Abstract: The aromaticity and local-aromaticity of a large set of polycyclic aromatic hydrocarbons (PAHs) is studied using multicenter delocalization indices from generalized population analysis and the popular nucleus independent chemical shift (NICS) index. A method for the fast computation of the NICS values is introduced, using the so-called pseudo- π -method. A detailed examination is made of the multidimensional nature of aromaticity. The lack of a good correlation between the NICS and the multicenter delocalization indices is reported and the grounds discussed. It is shown through a thorough statistical analysis that the NICS values arise not only from local aromaticity of the benzenoid rings, but also from other circuits. It is shown that the NICS indices do not reveal the individual aromatic nature of a specific ring, contrary to the delocalization indices.

© 2007 Wiley Periodicals, Inc. J Comput Chem 29: 358–366, 2008

Key words: aromaticity; local-aromaticity; generalized population analysis; NICS; chemical bond

Introduction

The so-called conceptual approach to chemistry has been extremely successful, and as a consequence many of these concepts play a dominant role in chemical reasoning. Examples are ubiquitous, and are likely to remain within chemical speech and reasoning for a long time to come. Paradoxically, many of these concepts do not have a very clear definition. As a consequence of this lack of a proper definition, concepts are used in a rather loose sense. Examples of such problematic concepts are the chemical bond, the definition and even the presence of atoms in molecules^{1–4} and many more. Probably one of the most dramatic examples is aromaticity.^{5–7} Although every chemist has some appreciation and understanding of the concept, there is still no conclusive definition, and as a consequence different workers in the field have a slightly different understanding. This naturally hampers attempts to quantify such a concept.

Nevertheless, there have already been numerous attempts to quantify molecular aromaticity and even local aromaticity. Local aromaticity in the context of the present paper refers to the degree of aromaticity of a fragment of a molecule, typically the degree of aromaticity of a specific benzenoid ring in a polyaromatic hydrocarbon. As there exists no conclusive definition of aromaticity, different indices have been introduced to measure aromaticity.^{6,7} These include geometry-based indices,⁸ molecular similarity of a benzenoid ring in a molecule to isolated benzene, including the well-known Polansky index,^{9,10} electron occupation numbers and

graph theory-based indices,¹¹ resonance energies,⁵ aromatic stabilization energy,¹² and many more. Intuitively, on the basis of the above mentioned more or less common understanding of molecular aromaticity one would expect that all these indices correlate more or less well. Surprisingly, this is not the case. Within e.g., the group of aromatic molecules, different indices may very well attribute different degrees of aromaticity to the same molecules. The fact that all indices are widely accepted as reflecting a degree of aromaticity and the fact that they do not correlate mutually, has resulted in the acceptance of aromaticity as a so-called multidimensional concept.^{12–15}

In the present paper, the correlation is examined between a magnetic index of aromaticity and an index based on the extent of electron delocalization. It is well-known that aromatic compounds exhibit special magnetic properties.⁵ The most prominent effect is

Cartesian coordinates of the PAHs used in this study as well as their total SCF energy, charge and multiplicity are available as supplementary material, together with a graphical representation of their σ -framework

This article contains supplementary material available via the Internet at <http://www.interscience.wiley.com/jpages/0192-8651/suppmat>

Correspondence to: P. Bultinck; e-mail: patrick.bultinck@ugent.be

Contract/grant sponsors: Ghent University; Institute for the Promotion of Innovation through Science and Technology (IWT PhD grant); The fund for Scientific Research, Flanders, Belgium

the occurrence of diatropic ring currents in aromatic molecules. These ring currents lie at the basis of the so-called nucleus independent chemical shift (NICS) index,^{16,17} used often to quantify (local) aromaticity. Ring currents arise under the presence of an external magnetic field and in turn cause an induced magnetic field. The nuclear shielding tensor σ is the negative proportionality factor between the electronically induced magnetic field, taken at the atomic position, and the externally applied one.¹⁸ The NICS correspond to the negative of either the trace or some component, depending on the version of NICS used, of this tensor computed at some point in space. NICS are nucleus independent since these points usually do not coincide with a certain nucleus. Most often they are computed at the center of an aromatic ring, assuming that their value in this single point is a measure of the size of the ring current in this ring. This means that all information of the entire ring current is somehow considered reflected in a single point, an approach which has been heavily criticized.^{19–22} Nevertheless, the practice of computing NICS values in the center of an aromatic ring as an index of the degree of aromaticity is common practice.

One of the key features of aromaticity is that there needs to be a delocalized electronic system.⁵ This means that electrons are delocalized over e.g., the six carbon atoms constituting the benzene ring. Many approaches have been published before on ways to measure this extent of electron delocalization. Among these are those based on higher order density functions. In recent years, several such indices have been developed, most notable are the PDI (para delocalization index)^{23,24} and the FLU (fluctuation) indices.^{24,25} Both of these are based on using only bond indices between two atoms at a time. In all cases these bond indices are essentially based on the Wiberg–Giambiagi–Mayer scheme,^{26–29} although sometimes extended to include other types of population analyses instead of the original Mulliken one.^{30,31} In the PDI the average bond index between each two atoms in para position is used as an index. In the FLU index, only the bond indices of all couples of covalently bonded atoms is used. We have recently extended the so-called generalized population analysis (GPA)^{32–34} for quantifying aromaticity in six-membered rings via computing the so-called six center index (SCI)^{31,35,36}:

$$SCI = \sum_{\nu \in A} \sum_{\mu \in B} \dots \sum_{\xi \in F} \sum_i \Gamma_i [(\mathbf{PS}_{\nu\mu})(\mathbf{PS}_{\mu\lambda}) \dots (\mathbf{PS}_{\psi\xi})(\mathbf{PS}_{\xi\nu})] \quad (1)$$

Here \mathbf{P} is the charge and bond order density matrix and \mathbf{S} is the overlap matrix of the basis functions. The labels A–F refer to the atoms contained in the ring considered, greek symbols refer to the basis functions, and Γ_i is a permutation operator that generates $5!$ terms by interchanging the Greek basis function labels μ to ξ . This index can be extended to Bader's Atoms in Molecules theory^{1–3} in a straightforward way.^{30,31} Also, the GPA indices for smaller or larger rings are easily derived by analogy to eq. (1).

As mentioned earlier, aromaticity is often considered a multidimensional property.^{12–15} This means that indices could, in principle, reflect the same general concept and still not correlate well mutually. The purpose of the present paper is to examine the correlation between GPA-based multicenter indices on the one hand and NICS on the other hand. As will be reported below, there is no significant

correlation. The second aim of the paper is then to study in detail the correlation and to examine whether there exists also a local version of the earlier mentioned multidimensionality. The lack of correlation is then explained by purely chemical reasoning. After the hypothesis has been developed, an in-depth statistical study is made to see whether the hypothesis is supported quantitatively.

As a molecular set, a large number of polycyclic aromatic hydrocarbons (PAH) are used. The reason for using these molecules is that they are known to be aromatic compounds, but the many different geometries notably change the aromaticity of the individual rings, depending on their place in the molecule. There has already been quite some discussion of the performance of NICS for the quantification of local aromaticity in the PAHs, especially for the central rings of anthracene and other linear acenes.^{19,31,37–41} NICS consistently make the central rings of linear acenes more aromatic than those on the outer edges of the acenes, and often make them more aromatic than benzene itself. Nevertheless, linear polyacenes are commonly known to become more reactive with an increasing number of rings and are known to be more reactive towards the inner rings, suggesting a decrease of aromatic character. The NICS-values however increase towards the inner rings, suggesting an increase in aromaticity, contradicting the experiment. Because of this contradiction the NICS data for the linear acenes have been met with scepticism,^{19,31,37,38} although according to Schleyer et al., one should not use chemical reactivity as an aromaticity criterion.⁴¹ The SCI predicts a reverse trend in the local aromaticity of these rings.^{31,35,42} In a recent contribution it was claimed that this contradiction would be due to the influence of different higher-order circuits on the NICS rather than the local (benzenoid) aromaticity alone.⁴³ In anthracene, for example, there are three of these higher-order aromatic circuits (D to F in Fig. 1) which could contribute to the NICS-value. The SCI on the other hand only describes the

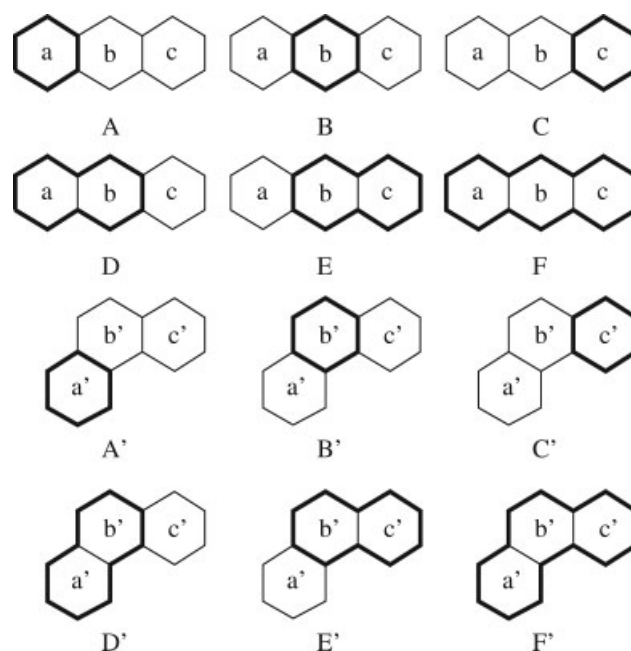


Figure 1. The different 6-, 10-, and 14-center circuits in anthracene and phenanthrene.

benzenoid aromaticity. In this contribution it will be shown that using the multicenter bond indices the NICS values can be broken up into the different 6-, 10-, and 14-center contributions.

The problem of separating the contributions of different current paths has already been handled by some other research-groups. Anusooya et al. calculated the ring currents for polyacenes along different circulation paths, using the Pariser–Parr–Pople π -electron model.³⁸ Aihara et al. used topological resonance energies and bond resonance energies built on graph theory to calculate current density maps and the contribution for different circuits in linear polyacenes.³⁷ In a different publication, the same author presented the graph theoretical circuit resonance energies for all circuits of 10 PAHs and the current density maps obtained by superposing the currents of the individual circuits.⁴⁴ In a previous contribution we have shown that the values of the sixfold delocalization (the local sixfold aromaticity) of these contributions correlate highly with the SCI.⁴³

The interest in calculating the aromatic properties of larger sets and systems has recently brought back the 1937 idea of London who discussed the analogy between the benzene current in the π -system and that of a system build up by six hydrogen atoms replacing the carbon atoms.⁴⁵ This so called pseudo- π method has proven to be surprisingly accurate in describing the ring currents⁴⁶ and in calculating the multi center bond indices⁴⁷ of PAHs. Using this pseudo- π -method it is possible to reduce the computer time drastically, allowing the calculation of the properties of increasingly larger systems.⁴⁸ In this contribution it will also be shown that the pseudo- π -method is accurate in calculating the popular NICS values for the PAHs, providing us with a useful tool for the fast calculation of these values.

Computational Methods

To have a sufficiently wide set of data of PAH NICS and SCI values, 108 PAH molecules ranging from benzene, naphthalene, anthracene, phenanthrene to 104 benzenoids with four, five, and six rings were used. The molecular set contains a total of 493 symmetry-unique rings and is available as supporting information. In a first approach, all molecular geometries were constructed from Z-matrices with C–C bond lengths equal to 1.4 Å and C–H bond lengths equal to 1.1 Å. Bond angles and dihedral angles were frozen to standard values, so that the molecules are considered planar and the highest symmetry is obtained for all PAHs. In a second approach, the molecules were optimized with the constraint of planarity. All optimizations were carried out at the B3LYP/6-311G** level using Gaussian-03.⁴⁹ NICS were evaluated at the centers of the aromatic rings and 1 Å above the rings. Multicenter indices were computed according to eq. (1), using the pseudo- π method (*vide infra*).

Over time, different kinds of NICS indices have appeared.^{17,50,51} Originally, they were computed at the center of the rings and the trace of the chemical shift tensor was used as an index. In a later stage, it was suggested that NICS should be computed at 1 Å above the center of the ring to reflect better the π component of the NICS.⁵⁰ Fowler et al. pointed out the tensor character of the chemical shift and consequently that only the σ_{zz} should be used.^{20,21} More recently, it is advised to use yet another NICS approach, where the σ_{zz} is computed for only the π orbitals.^{21,52} To avoid computational burden and difficulties, especially for the larger molecules, an alternative calculation scheme is developed below, based on the

so-called pseudo- π algorithm. This gives chemical shifts for only the π electron density and also allows computing the multicenter indices in a much more efficient way. In this contribution the NICS(0), NICS(1), and their zz -components were calculated using the B3LYP functional and the 6-311G** basis set and the pseudo- π approximation.

Multicenter indices were computed using the in home developed Kekule program which uses the Gaussian-03⁴⁹ formatted checkpoint file. As will be shown below, multicenter indices were computed for the benzenoid circuits containing six atoms (SCI), naphthalene-like circuits containing 10 atoms (TCI) and 14-membered circuits either with all three rings in a linear sequence (FCI-a) or in an angular sequence (FCI-b) (Fig. 1).

For the study of correlations between the NICS and multicenter indices, the ARTE-QSAR program was used.⁵³ This program allows deriving regressions and correlations with main focus on the statistical validity and allows to establish the domain of applicability of the regressions found.

Results and Discussion

The Pseudo- π Approach

It has long been established that there is a very large analogy between the π MOs of benzene and the MOs produced by an array of only s orbitals.⁴⁵ This analogy lies at the heart of the pseudo- π method. This method has been revived in aromaticity studies by Fowler et al. to allow for a substantial reduction in the computational cost of ring current calculations.⁴⁶ The pseudo- π approach in the present study essentially involves three steps:

- If needed, the geometry of the PAH is optimized at some desired level of theory, considering all C and H atoms but constraining the geometry to planarity.
- After this optimization all hydrogen atoms are removed from the previous structure. The carbon atoms of molecular skeleton are subsequently replaced by hydrogen atoms at the same coordinates.
- An *ab initio* calculation is performed using HF/STO-3G calculations for this hydrogen network.

In case of frozen geometries, of course one can skip the first step and proceed immediately to the second step. As discussed in detail by Fowler et al., there is a one-to-one relationship between the MOs obtained from the *ab initio* calculation with the entire molecule and the ones from the hydrogen network calculation. As a consequence, the ring current maps are also very similar, not only qualitatively but even quantitatively.^{46,54}

For the present study, the validity of the pseudo- π method for the computation of NICS and multicenter indices needs to be established. For the multicenter indices, the pseudo- π approach has already been shown to allow a very fast and accurate calculation of both the PDI and SCI indices.⁴⁷ For the SCI indices the correlation coefficient between the full molecular indices and the pseudo- π indices amounts nearly 99%. Also it was found that the effect on the SCI of clamping benzenoid rings is the same, independent of using the full molecular calculation or the pseudo- π approach.⁴⁷ Moreover, as the number of basis functions in a pseudo- π calculation

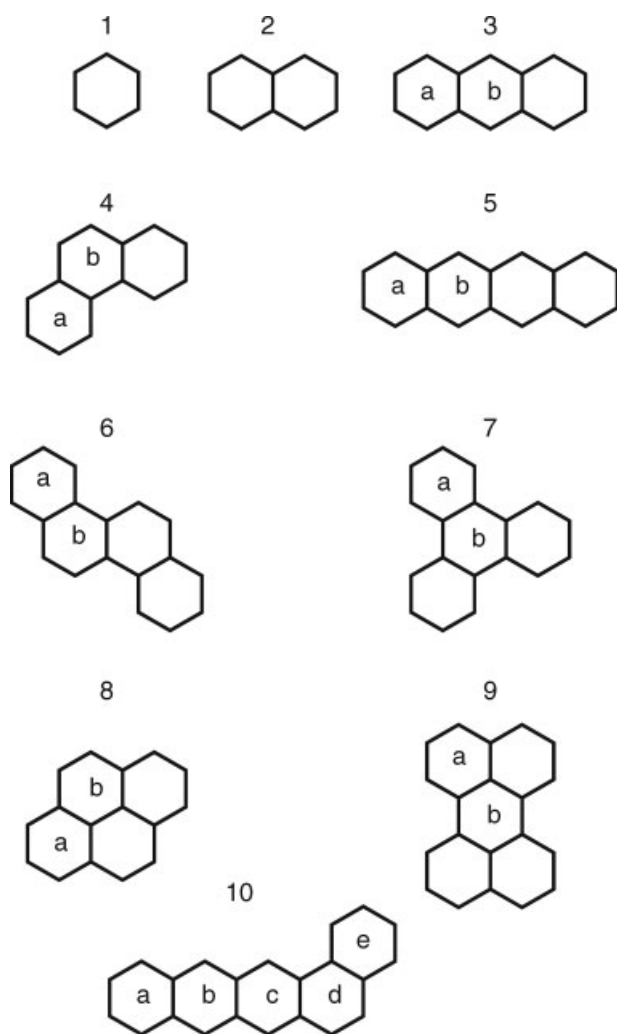


Figure 2. Some common PAH, included in this study. Only the σ -framework is shown.

is much smaller than in a complete molecular calculation, it becomes tractable to compute delocalization indices for larger rings. The pseudo- π method thus allows computing also the TCI as well as the FCI-a and FCI-b.

No test has yet been performed on the applicability of the pseudo- π method for the computation of the NICS indices. First we will look at the correlation between the NICS and pseudo- π -NICS (PP-NICS). The different values of the NICS and PP-NICS of some common PAH's (Fig. 2) are presented in Table 1. From this data it is seen that the PP-NICS mimic the trends in the NICS values. The correlations between the different types of NICS are summarized in Table 2. These are the correlations for 499 symmetry unique rings of 113 molecules, including the cyclopentadienyl anion, the tropylium ion, azulene, and the fluorene anion to incorporate some five- and seven-membered rings, calculated on the frozen ideal geometry. All NICS and PP-NICS-values are significantly correlated, with the R^2 -values above 0.9. Since the pseudo- π method mimics the π -system of the molecules, one would expect the NICS(1) to be in better correlation with the PP-NICS than the NICS(0). This is indeed

confirmed by our calculations, for which the R^2 -values are slightly bigger. From these correlations it is also seen that the more aromatic-sensitive NICS(1) and the NICS_{ZZ} give slightly better correlations with the PP-NICS_{ZZ}.

From these findings it is clear that the PP-NICS are a worthy alternative to the complete NICS-calculations.

Non-Local Contributions to the NICS

Having established an algorithm that allows computing efficiently the NICS and multicenter aromaticity indices, it is worth examining the correlation between both sets of indices. The correlation coefficient amounts only 38%. Figure 3 shows the predicted NICS, based on the SCI alone on one hand and the actual, computed NICS on the other. The predicted NICS are obtained by the regression equation between the actual NICS and the SCI. This may be seen as a confirmation of the multidimensional nature of aromaticity. Yet, merely observing this fact is not sufficient as such a poor correlation can indicate nothing but a total failure of the aromaticity concept.

The situation, however, is not so drastic. It has been reported before that in some cases there is no multidimensionality between the NICS and Multicenter Bond indices. As an example, Bultinck et al. found that for homo-aromatic systems, there is a good correlation between NICS and multicenter indices and that these regressions are equally valid for classical five membered aromatic molecules such as thiophene, pyrrole, . . .⁴² The lack of correlation thus apparently appears when molecules contain several aromatic rings.³⁵ This is in line with observations by Stanger et al.¹⁹ or Solà and co-workers.^{55–57}

Turning back to ring currents, it is well-known that one can consider different circuits as contributors to the total ring current.^{37,44} As an example, anthracene contains six different aromatic circuits (Fig. 1). Three of them correspond to benzenoid circuits, two naphthalene-like circuits, and one circuit that follows the edge of the entire molecule. The ring current $j(\mathbf{r})$ in every point in the molecule can be considered as arising from the different circuits.²² In anthracene, using the notation used in Figure 1, one can write:

$$j(\mathbf{r}) = j_A(\mathbf{r}) + j_B(\mathbf{r}) + j_C(\mathbf{r}) + j_D(\mathbf{r}) + j_E(\mathbf{r}) + j_F(\mathbf{r}) \quad (2)$$

The proposed use of NICS as a local aromaticity criterion for a specific benzenoid ring would rely implicitly on the assumption that for example on the center of the ring A, the contributions from circuits B-F would be zero or cancel completely. Such cancellation is not guaranteed at all. As has been stated before by Bultinck et al., the more negative NICS value in the center of the inner ring may very well be due to the fact that this point is encircled by more aromatic circuits, rather than that $j_B(\mathbf{r}_B) > j_A(\mathbf{r}_A)$.⁴³

Analogous to eq. (2), one could suggest also that the NICS computed at a certain point originates from all circuits in a molecule, or:

$$\text{NICS}(\mathbf{r}) = \text{NICS}_A(\mathbf{r}) + \text{NICS}_B(\mathbf{r}) + \text{NICS}_C(\mathbf{r}) + \text{NICS}_D(\mathbf{r}) + \text{NICS}_E(\mathbf{r}) + \text{NICS}_F(\mathbf{r}) \quad (3)$$

Given the fact that the NICS indices for single ring molecules seem to usually correlate quite well with the multicenter index for

Table 1. The Different NICS and PP-NICS-Values of Some Common PAH (Fig. 2).

Molecule	Ring	NICS(0)	NICS(1)	NICS _{ZZ} (0)	NICS _{ZZ} (1)	PP-NICS	PP-NICS _{ZZ}	SCI
1		−8.73	−10.98	−14.17	−28.91	−17.49	−41.21	100
2		−9.23	−11.55	−13.79	−29.76	−17.14	−40.34	55
3	<i>a</i>	−8.52	−11.02	−11.48	−27.95	−15.95	−36.90	42
	<i>b</i>	−11.34	−13.37	−17.98	−34.43	−19.34	−46.99	38
4	<i>a</i>	−8.91	−11.33	−12.27	−28.85	−17.49	−41.07	66
	<i>b</i>	−6.64	−9.69	−3.97	−23.09	−13.31	−29.11	25
5	<i>a</i>	−7.92	−10.53	−9.58	−26.38	−15.02	−34.16	37
	<i>b</i>	−11.37	−13.45	−17.90	−34.49	−19.25	−46.83	32
6	<i>a</i>	−8.86	−11.30	−12.03	−28.67	−17.40	−40.82	62
	<i>b</i>	−7.00	−10.04	−4.47	−23.90	−14.54	−32.47	31
7	<i>a</i>	−7.64	−10.32	−8.00	−25.57	−16.86	−38.94	73
	<i>b</i>	−2.95	−6.99	9.29	−13.89	−8.53	−15.10	11
8	<i>a</i>	−11.65	−13.77	−19.73	−35.81	−20.20	−49.27	52
	<i>b</i>	−4.65	−8.22	1.96	−18.60	−10.69	−20.98	25
9	<i>a</i>	−5.10	−8.23	0.17	−19.04	−14.95	−33.41	49
	<i>b</i>	8.19	2.15	42.68	13.75	3.37	20.64	8
10	<i>a</i>	−8.25	−10.86	−10.59	−27.23	−15.50	−35.55	39
	<i>b</i>	−11.34	−13.48	−17.72	−34.31	−19.43	−47.28	34
	<i>c</i>	−10.05	−12.48	−13.47	−31.06	−18.12	−43.17	34
	<i>d</i>	−3.78	−7.40	4.94	−15.72	−9.67	−18.43	16
	<i>e</i>	−8.31	−10.83	−10.29	−27.06	−17.13	−39.87	70

The SCI value is the pseudo- π -value in benzene-%.

the ring involved,⁴² one could suggest the following hypothesis. Suppose that for each circuit one has a similar correlation between the NICS contribution and the multicenter index for that circuit. For example in anthracene (Fig. 1), this supposes:

$$\text{NICS}_A(\mathbf{r}) \sim \text{SCI}_A \quad (4)$$

$$\text{NICS}_D(\mathbf{r}) \sim \text{TCI}_D \quad (5)$$

$$\text{NICS}_F(\mathbf{r}) \sim (\text{FCI-a})_F \quad (6)$$

Then the total NICS at the center of some ring X could be written in terms of the SCI, TCI, FCI-a, and FCI-b via a linear relationship:

$$\text{NICS}(\mathbf{r}_X) = a\text{SCI} + b \sum_j \text{TCI}_j + c \sum_k \text{FCI-a}_k + d \sum_l \text{FCI-b}_l + C^{\text{te}} \quad (7)$$

In this regression line, the summations are limited to only those rings that effectively encircle the center of the ring X. This means that contributions from other circuits more distant from the ring center

are not considered. As Schleyer et al. have shown, these are indeed quite small and thus can be neglected in the regression above.⁴¹

FCI-a and FCI-b are the 14-center indices in the linear sequence and the angular sequence respectively (F and F' in Fig. 1). One might, however, postulate that since the linear and angular FCI are both indices for 14-center-delocalizations, they should have an equal contribution to the NICS. Separating the anthracene and the phenanthrene circuit might then just be a unnecessary degree of freedom in the model. In this line of thought one could take the sum of the FCI-a and FCI-b and treat it as a total FCI. Both approaches will be studied throughout this contribution.

Statistical Verification

Using the NICS and multicenter index data obtained from the pseudo- π calculations, the linear regression from eq. (7) was performed. In a first step, frozen geometries were used. This constraint will be released later in the study.

For any statistical model, first it should be checked what is the Topliss ratio of the regression,⁵⁸ this is the ratio of the number of molecules over the number of selected descriptors. In the present application, 3 or 4 regression coefficients are used. This gives a very favourable Topliss ratio as there are 496 data points. This means that for every coefficient there are more than 100 data points. As a reference for the quality of this ratio, one can mention that the European Union guidelines for good QSAR practice recommend Topliss ratios of at least 5 and preferably 8.⁵⁹

The NICS were fitted to the SCI, TCI and FCI using eq. (7), and the constants *a*, *b*, *c*, and *d* were calculated. This was done for the NICS(0), NICS(1), the NICS_{ZZ}(0), the NICS_{ZZ}(1), the PP-NICS and the PP-NICS_{ZZ} on the ideal frozen geometries, and for the PP-NICS and the PP-NICS_{ZZ} on the optimized planar geometries. The *R*² values between the different NICS-values and the NICS

Table 2. The Correlations Between the Different Types of NICS Values.

<i>R</i> ²	PP-NICS	PP-NICS _{ZZ}
NICS(0)	0.929	0.932
NICS(1)	0.938	0.942
NICS _{ZZ} (0)	0.952	0.958
NICS _{ZZ} (1)	0.947	0.952

Table 3. The R^2 and q^2 Values Between the Different NICS-Values and the NICS Predicted by the Models with FCI-a and FCI-b Contributions Separate and Together (FCI).

R^2 (q^2)	FCI-a and FCI-b	FCI
NICS(0)/FRO	0.862 (0.860)	0.847 (0.845)
NICS(1)/FRO	0.857 (0.854)	0.839 (0.837)
NICS _{ZZ} (0)/FRO	0.862 (0.859)	0.836 (0.834)
NICS _{ZZ} (1)/FRO	0.857 (0.855)	0.837 (0.835)
PP-NICS/FRO	0.906 (0.905)	0.891 (0.890)
PP-NICS _{ZZ} /FRO	0.902 (0.900)	0.885 (0.884)
PP-NICS/OPT	0.922 (0.921)	0.896 (0.894)
PP-NICS _{ZZ} /OPT	0.916 (0.915)	0.887 (0.886)

FRO indicates that the values have been calculated on frozen geometries, OPT that they have been calculated on optimized geometries.

predicted by the models are presented in Table 3. All values show a significant correlation around 0.84 and above. When comparing the two methods there is only a slight improvement seen when taking the FCI-a and FCI-b as separate descriptors. Apparently in each model the NICS values and the NICS_{ZZ} values are equally well correlated with the values obtained by the linear relation of the multicenter-indices. The pseudo- π -values seem to be better predictable than the classical NICS. This might be due to a better one-to-one correspondence with the actual π -electron delocalization, by elimination of the σ -framework. The PP-NICS_{ZZ} values predicted by both models, compared to the actual value for some common PAH's (Fig. 2) are shown in Tables 4 and 5.

From these values it is clear that the trend and magnitude of the NICS are predicted quite well by the models. The mean absolute difference between the actual PP-NICS_{ZZ} values and the ones given by the models for all 496 symmetry unique rings is around 2.9 ppm. The comparison of these 496 PP-NICS_{ZZ} values with the ones obtained by both models are shown graphically in Figures 4 and 5. The very favorable correlation is manifest if compared with the predicted PP-NICS based on only the SCI (Fig. 3).

Using the linear model one can assess the magnitude of the different contributions to the NICS. One might expect the six-center contribution (SCC) to the NICS to be the largest, followed by the 10-center contribution (TCC) and the 14-center contribution (FCC). The different contributions to the PP-NICS_{ZZ} values within the models are also given in Tables 4 and 5. When examining the different contributions to the NICS one has to bear in mind that the model-NICS is not just the sum of the 6-, 10-, and 14-center contributions (SCC, TCC, FCC), but that there is still the constant in eq. (7) which is around 23 ppm. By looking at the contributions for the different members of the NICS-family it was found that, as expected, the SCC is the largest, with an average of about 50% of the total sum of the SCC, TCC, and FCC, followed by the TCC with about 32% and finally the FCC with about 18% of the total. In those models where the FCI-a and the FCI-b circuit are treated separately an average of about 9% was found for both circuits. As it seems that larger circuits have a continuously lowering impact on the predicted NICS, one can expect that higher order circuits have even smaller contributions to the NICS. This is coherent with the fact that for larger polyacenes, the NICS values seem to converge to a limit value rather than to increase continuously.

Table 4. The PP-NICS_{ZZ} Value Predicted by the Model, the Different Contributions to This Value and Its Actual Value for the Model with FCI-a and FCI-b Contributions Separate (St-E is the Standard Error on the Model-PP-NICS_{ZZ}).

Molecule	Ring	PP-NICS _{ZZ}	SCC	TCC	FCC-a	FCC-b	Model-PP-NICS _{ZZ}	St-E
1		-41.21	-70.28	-	-	-	-47.60	±1.38
2		-40.34	-38.43	-26.91	-	-	-42.66	±1.79
3	a	-36.90	-29.59	-17.46	-18.49	-	-42.86	±2.05
	b	-46.99	-26.90	-34.91	-18.49	-	-57.62	±2.59
4	a	-41.07	-46.10	-12.41	-	-10.95	-46.78	±1.94
	b	-29.11	-17.56	-24.82	-	-10.95	-30.66	±1.92
5	a	-34.16	-26.12	-14.21	-13.34	-	-30.99	±1.69
	b	-46.83	-22.67	-27.18	-26.68	-	-53.86	±2.59
6	a	-40.82	-43.78	-15.73	-	-5.35	-42.18	±1.75
	b	-32.47	-22.10	-21.85	-	-10.71	-31.98	±1.88
7	a	-38.94	-51.08	-5.34	-	-9.11	-42.85	±1.70
	b	-15.10	-7.90	-16.01	-	-13.67	-14.90	±1.61
8	a	-49.27	-36.75	-19.29	-	-18.52	-51.88	±2.39
	b	-20.98	-17.41	-21.56	-	-9.26	-25.55	±1.73
9	a	-33.41	-34.73	-22.56	-0.87	-0.73	-36.21	±1.66
	b	20.64	-5.39	-7.23	-1.74	-1.46	6.85	±0.76
10	a	-35.55	-27.62	-15.42	-14.43	-	-34.80	±1.80
	b	-47.28	-24.17	-29.23	-19.94	-	-50.65	±2.42
	c	-43.17	-23.70	-19.66	-19.94	-5.14	-45.76	±2.33
	d	-18.43	-11.44	-13.58	-5.51	-5.14	-12.99	±1.39
	e	-39.87	-49.31	-7.72	-	-5.14	-39.50	±1.56
Average			49.90%	31.30%	8.10%	10.70%		±1.69

Table 5. The PP-NICS_{ZZ} Value Predicted by the Model, the Different Contributions to This Value and Its Actual Value for the Model with FCI-a and FCI-b Contributions Together (FCC) (St-E is the Standard Error on the Model-PP-NICS_{ZZ}).

Molecule	Ring	PP-NICS _{ZZ}	SCC	TCC	FCC	Model-PP-NICS _{ZZ}	St-E
1		−41.21	−68.96	−	−	−45.80	±1.98
2		−40.34	−37.70	−28.75	−	−43.29	±2.40
3	<i>a</i>	−36.90	−29.03	−18.65	−14.29	−38.81	±2.66
	<i>b</i>	−46.99	−26.39	−37.31	−14.29	−54.83	±3.20
4	<i>a</i>	−41.07	−45.23	−13.26	−12.66	−47.99	±2.55
	<i>b</i>	−29.11	−17.23	−26.52	−12.66	−33.25	±2.53
5	<i>a</i>	−34.16	−25.62	−15.18	−10.31	−27.96	±2.30
	<i>b</i>	−46.83	−22.25	−29.04	−20.62	−48.75	±3.19
6	<i>a</i>	−40.82	−42.95	−16.80	−6.19	−42.79	±2.36
	<i>b</i>	−32.47	−21.69	−23.35	−12.38	−34.25	±2.49
7	<i>a</i>	−38.94	−50.12	−5.70	−10.53	−43.20	±2.30
	<i>b</i>	−15.10	−7.75	−17.10	−15.80	−17.50	±2.21
8	<i>a</i>	−49.27	−36.06	−20.62	−21.41	−54.92	±3.00
	<i>b</i>	−20.98	−17.08	−23.04	−10.70	−27.66	±2.34
9	<i>a</i>	−33.41	−34.07	−24.10	−1.52	−36.53	±2.26
	<i>b</i>	20.64	−5.29	−7.73	−3.03	7.11	±1.37
10	<i>a</i>	−35.55	−27.11	−16.47	−11.15	−31.57	±2.40
	<i>b</i>	−47.28	−23.71	−31.23	−15.41	−47.19	±3.02
	<i>c</i>	−43.17	−23.25	−21.01	−21.35	−42.45	±2.94
	<i>d</i>	−18.43	−11.23	−14.51	−10.20	−12.77	±1.99
	<i>e</i>	−39.87	−48.39	−8.25	−5.94	−39.42	±2.17
Average			48.50%	33.10%	18.40%		±2.30

Of course, statistical models should be substantiated by more than just correlation coefficients. A *t*-test reveals that all regression coefficients are indeed relevant, as their values are outside the range [−2; +2]. The F-test at the 0.95 confidence level for the significance of the total number of coefficients used is quite high, showing that the correlation reported is causal rather than fortuitous. As an internal validation, the leave-many-out procedure was carried out. In this procedure 40 points were left out from the derivation of the model. The coefficients of eq. (7) were determined with the remaining molecules. Using these coefficients, the value of the 40 points was predicted and the R^2 between the predicted and the actual NICS value was determined. This was done 100,000 times and the leave-many-out q^2 is computed. This value was found to be virtually equal to the R^2 indicating again a very meaningful correlation. It is gratifying that both for frozen geometries and optimized geometries the R^2 and q^2 are very similar, even with slightly higher values when using optimized geometries. As an alternative internal validation, the NICS values of all rings were randomly permuted 1000 times and a statistical model, including the determination of the q^2 , was developed after every permutation. The R^2 and q^2 for all permutations of the PP-NICS_{ZZ} is reported in Figure 6. This figure clearly shows again that the model reported above stands out of the other 1000 models. These figures are almost identical for all investigated NICS-values.

Meaning of the Local Aromaticity Concept

The question naturally arises on what information is conceptually contained in the value of multicenter indices and NICS. The local aromaticity concept was previously discussed in detail^{31,35,36,43,60}

and the present findings confirm that some of the multidimensionality arises not *per se* from multidimensionality but may also arise from the diffuseness of the definition of aromaticity and local aromaticity a fortiori.

NICS as a local aromaticity index may be seen to reflect at a chosen point all ring currents in the molecule. So when there are several circuits in a molecule, all of these will contribute to the NICS computed in some chosen point. NICS can not be used to assess a degree of benzenoid character for a specific ring in a PAH, as they not solely contain the ring current of the benzenoid circuit.

On the other hand, multicenter indices allow to reveal the degree of aromaticity in a certain circuit. Depending on the size of the circuit, an index can be computed allowing to compare its degree of aromaticity to another ring of the same size. Optionally, a normalization can be performed which allows even comparing rings of different sizes.⁶¹

So both indices reflect inherently different views of local aromaticity. It is very interesting to mention again that, indeed, if only one circuit is present, there are good correlations between both indices.⁴² Obviously, it would be very interesting if NICS could be dissected in the different circuit contributions schematically introduced in eq. (7). No such procedure exists at the *ab initio* level, unfortunately. Aihara et al.,^{37,44} as well as Anusooya et al.³⁸ did derive such a graph theoretical procedure and independently from us characterized the strength of different circuits in PAH via circuit specific ring currents or circuit resonance energies. Bultinck et al. have recently shown how extremely tight correlations are found between these dissected NICS and ring current intensities on the one hand and multicenter indices on the other hand.⁴³ This provides strong

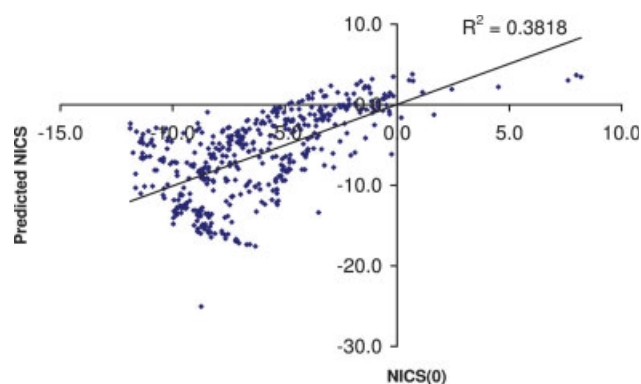


Figure 3. The regression between the NICS(0) and the NICS(0) predicted by the SCI-values.

arguments to show how the above regression may be considered chemically very meaningful.

Still, there may obviously appear cases where NICS show no correlation with the set of multicenter indices. In such cases, it will again prove very interesting to investigate the grounds for such a lack of adherence to the model. Such cases can be anticipated whenever the NICS approach is likely to produce results not in line with ring current maps. This is the case in e.g., bifurcated circuits.^{62,63} By the fact that NICS concentrate all ring current information in a single number at an arbitrarily chosen point, one is bound to lose quite a lot of information.⁶⁴ It is not possible to extract from NICS again the ring current information. As a consequence, ring current maps are superior to the NICS and it is clear that correlations between ring current maps and multicenter indices would be very interesting. Such research is currently being carried out.

Conclusions

It has been shown that the NICS index in its different versions and the General Population Analysis-based SCI do not show any meaningful correlation. The correlation found is so poor that it could hardly be attributed to the multidimensional nature of aromaticity.

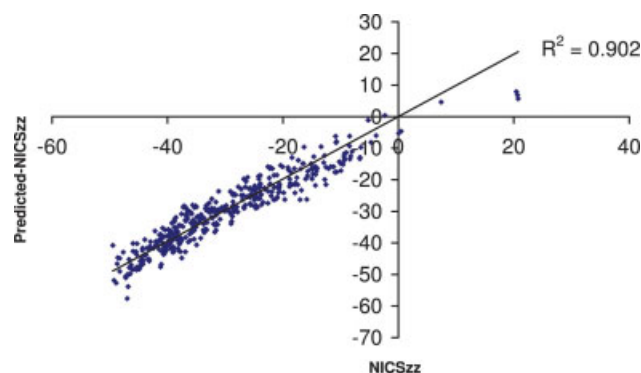


Figure 4. The regression between the *ab initio* computed PP-NICS_{zz} and the PP-NICS_{zz}-values obtained by regression, treating the FCI-a and FCI-b separate. The correlation depicted is based on frozen geometries. The correlation with optimized geometries has $R^2 = 0.916$.

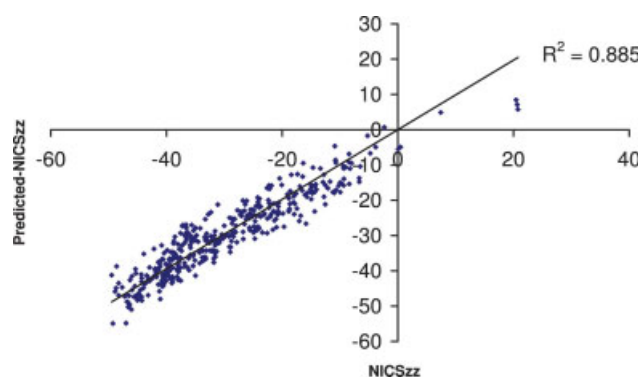


Figure 5. The regression between the *ab initio* computed PP-NICS_{zz} and the PP-NICS_{zz}-values obtained by regression, treating the FCI-a and FCI-b together. The correlation depicted is based on frozen geometries. The correlation with optimized geometries has $R^2 = 0.887$.

As NICS are related to ring currents and the global ring current can be considered as built from the different currents of all individual circuits in a molecule the hypothesis was put forward that the set of multicenter indices for all different circuits could correlate with the computed NICS values. Indeed, it was shown through thorough statistical analysis that the NICS values and combined multicenter indices for all individual circuits correlate very favorably. The correlation improvement amounts approximately 50%. The observed lack of correlation between NICS computed at a benzenoid ring center and the multicenter index for the benzenoid circuit infers that NICS should not be used to assess the degree of local aromaticity of a benzenoid circuit. Therefore, it should be avoided to report correlations between aromaticity indices reflecting strictly only a specific circuit and NICS values, even if computed at the center of that circuit as other circuits can strongly influence the NICS value.

In the course of this study we have shown that the pseudo- π -method is a trustworthy and computationally advantageous alternative to the 'complete' NICS calculation on PAH's. It might even be speculated that these values are a better tool to examine

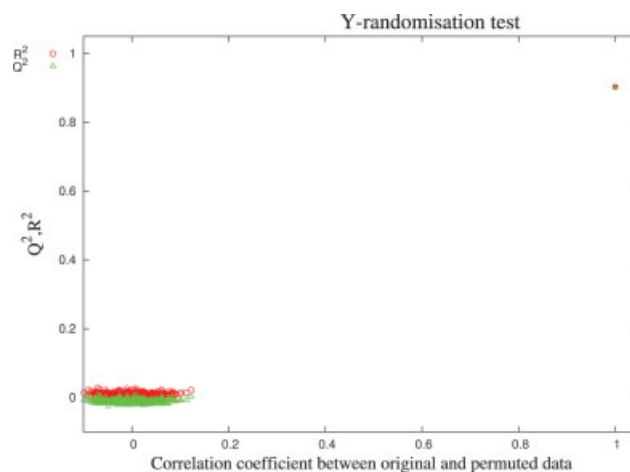


Figure 6. The q^2 (green) and R^2 (red) values for the PP-NICS_{zz} after random permutation the NICS of all rings, compared to the q^2 and R^2 value of the original model.

the properties of the π -electron cloud since there is no influence on these values from a σ -framework.

References

- Bader, R. *Atoms in Molecules: A Quantum Theory*; Clarendon: Oxford, 1990.
- Bader, R. *Chem Rev* 1991, 91, 893.
- Popelier, P. *Atoms in Molecules. An Introduction*; Pearson Education: London, 2000.
- Parr, R.; Ayers, P.; Nalewajski, R. *J Phys Chem A* 2005, 109, 3957.
- Minkin, V.; Glukhovtsev, M.; Simkin, B. *Aromaticity and Antiaromaticity*; Wiley Interscience: New York, 1994.
- Schleyer, P. *Chem Rev* 2001, 101, 1115.
- Schleyer, P. *Chem Rev* 2005, 105, 3433.
- Krygowski, T.; Cyrański, M. *Chem Rev* 2001, 101, 1385.
- Bultinck, P.; Ponec, R.; Gallegos, A.; Fias, S.; Van Damme, S.; Carbó-Dorca, R. *Croat Chem Acta* 2006, 79, 363.
- Polansky, O.; Derflinger, G. *Int. J Quantum Chem* 1967, 1, 379.
- Randic, M. *Chem Rev* 2003, 103, 3449.
- Cyrański, M.; Krygowski, T. M.; Katritzky, A. R.; Schleyer, P. v. R. *J Org Chem* 2002, 67, 1333.
- Jug, K.; Koster, A. M. *J Phys Org Chem* 1991, 4, 163.
- Katritzky, A. R.; Karelson, M.; Sild, S.; Krygowski, T. M.; Jug, K. *J Org Chem* 1998, 63, 5228.
- Katritzky, A. R.; Barczynski, P.; Musumarra, G.; Pisano, D.; Szafran, M. *J Am Chem Soc* 1989, 111, 7.
- Elser, V.; Haddon, R. *Nature* 1987, 325, 792.
- Schleyer, P.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. *J Am Chem Soc* 1996, 118, 6317.
- Atkins, P.; Friedman, R. *Molecular Quantum Mechanics*; Oxford University Press, 1997.
- Stanger, A. *J Org Chem* 2006, 71, 883.
- Fowler, P.; Steiner, E. *Mol Phys* 2000, 98, 945.
- Steiner, E.; Fowler, P.; Jenneskens, L. *Angew Chem Int Ed Engl* 2001, 40, 362.
- Lazzeretti, P. *Phys Chem Chem Phys* 2004, 6, 217.
- Poater, J.; Fradera, X.; Duran, M.; Solà, M. *Chem Eur J* 2003, 9, 400.
- Poater, J.; Duran, M.; Solà, M.; Silvi, B. *Chem Rev* 2005, 105, 3911.
- Matito, E.; Duran, M.; Solà, M. *J Chem Phys* 2005, 122, 014109.
- Wiberg, K. *Tetrahedron* 1968, 24, 1083.
- Giambiagi, M.; de Giambiagi, M.; Grempel, D.; Heymann, C. *J Chem Phys* 1975, 72, 15.
- Mayer, I. *Chem Phys Lett* 1983, 97, 270.
- Mayer, I. *Int J Quantum Chem* 1986, 29, 73.
- Bohicchio, R.; Ponec, R.; Torre, A.; Lain, L. *Theor Chem Acc* 2001, 105, 292.
- Bultinck, P.; Rafat, M.; Ponec, R.; Carbó-Dorca, R.; Popelier, P. *J Phys Chem A* 2006, 110, 7642.
- Ponec, R.; Uhlk, F. *Croat Chem Acta* 1996, 69, 941.
- Ponec, R.; Mayer, I. *J Phys Chem A* 1997, 101, 1738.
- Ponec, R.; Cooper, D. *Int J Quantum Chem* 2004, 97, 1002.
- Bultinck, P.; Ponec, R.; Van Damme, S. *J Phys Org Chem* 2005, 18, 706.
- Bultinck, P.; Ponec, R.; Carbó-Dorca, R. *J Comput Chem* 2007, 28, 152.
- Aihara, J.; Kanno, H. *J Phys Chem A* 2005, 109, 3717.
- Anusooya, Y.; Chakrabarti, A.; Pati, S. K.; Ramasesha, S. *Int J Quantum Chem* 1998, 70, 503.
- Portella, G.; Poater, J.; Bofill, J.; Alemany, P.; Solà, M. *J Org Chem* 2005, 70, 2509.
- Poater, J.; Bofill, J.; Alemany, P.; Solà, M. *J Phys Chem A* 2005, 109, 10629.
- Schleyer, P. v. R.; Manoharan, M.; Wang, Z.-X.; Kiran, B.; Jiao, H.; Puchta, R.; Hommes, N. E. *Org Lett* 2001, 3, 2465.
- Ponec, R.; Bultinck, P.; Gallegos, A. *J Phys Chem A* 2005, 109, 6606.
- Bultinck, P.; Fias, S.; Ponec, R. *Chem Eur J* 2006, 12, 8813.
- Aihara, J. *J Am Chem Soc* 2006, 128, 2873.
- London, F. *J Phys Radium* 1937, 8, 397.
- Fowler, P. W.; Steiner, E. *Chem Phys Lett* 2002, 364, 259.
- Bultinck, P.; Mandado, M.; Mosquera, R. *J Math Chem* 2007, Published online, DOI:10.1007/s10910-006-9184-8.
- Fias, S.; Bultinck, P. *Faraday Discuss* 2007, 135, 381.
- Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision b.03. Gaussian: Pittsburg, PA, 2003.
- Schleyer, P. v. R.; Jiao, H.; Hommes, N. J. R. v. E.; Malkin, V. G.; Malkina, O. *J Am Chem Soc* 1997, 119, 12669.
- Fallah-Bagher-Shaidaei, H.; Wannere, C.; Corminboeuf, C.; R., P.; Schleyer, P. *Org Lett* 2006, 8, 863.
- Corminboeuf, C.; Heine, T.; Seifert, G.; Schleyer, P. v. R. *Phys Chem Chem Phys* 2004, 6, 273.
- Van Damme, S.; Bultinck, P. *J Comput Chem* 2007, 28, 1924.
- Monaco, G.; Viglione, R.; Zanasi, R.; Fowler, P. *J Phys Chem A* 2006, 110, 7447.
- Poater, J.; García-Cruz, I.; Illas, F.; Solà, M. *Phys Chem Chem Phys* 2004, 6, 314.
- Poater, J.; Solà, M.; Viglione, R. G.; Zanasi, R. *J Org Chem* 2004, 69, 7537.
- Osuna, S.; Poater, J.; Bofill, J. M.; Alemany, P.; Solà, M. *Chem Phys Lett* 2006, 428, 191.
- Topliss, J.; Edwards, R. *J Med Chem* 1979, 22, 1238.
- Worth, A.; Bassan, A.; Gallegos, A.; Netzeva, T.; Patlewicz, G.; Pavan, M.; Tsakovska, I.; Vracko, M. *The Characterisation of (Quantitative) Structure-Activity Relationships: Preliminary Guidance*; European Chemicals Bureau, Report EUR 21866 EN, 2005.
- Bultinck, P. A. *Faraday Discuss* 2007, 135, 347.
- Mandado, M.; González-Moa, M.; Mosquera, R. A. *J Comput Chem* 2007, 28, 127.
- Steiner, E.; Fowler, P. W. *Chem Phys Chem* 2002, 3, 114.
- Steiner, E.; Soncini, A.; Fowler, P. W. *Org Biomol Chem* 2005, 3, 4053.
- Soncini, A.; Steiner, E.; Fowler, P. W.; Havenith, R. W. A.; Jenneskens, L. W. *Chem Eur J* 2003, 9, 2974.