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Mutual relationships between magnetic aromaticity indices of heterocyclic compounds

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ABSTRACT: For three sets of aromatic compounds, namely various five-membered heterocycles, derivatives of 2*H*-tetrazole and six-membered heterocycles, a number of the aromaticity indices, especially magnetic ones, were calculated. The tables of correlation coefficients between the individual indices revealed that mutual relationships between them depend on their composition in the set and that some magnetic characteristics themselves may be orthogonal to others. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: aromaticity indices; heterocycles; tetrazole derivatives; magnetic properties

INTRODUCTION

It has now been generally accepted that aromaticity neither is a physical observable nor can be characterized by any single well-defined, measurable or calculated parameter.[1–3] Instead, aromaticity is evaluated employing a wide set of parameters relating to different molecular properties. As a recent development, new electronic aromaticity criteria, reflecting delocalization of the π system, have been added to the structural, energetic and magnetic properties formerly used.[4] They are applied to estimate the extent of transfer of electron density from the p_z orbital of the heteroatom to the rest of the π system, LP[5] (for heteroaromatic, five-membered compounds) or a standard deviation of electron density inside the ring, SDn.[6]

The present definition of aromaticity proposes that an aromatic compound is a species possessing the ability to sustain an induced ring current.[7,8] Neither aromaticity itself nor ring current are physical observables. Meanwhile, the concept of ring current due to π electron delocalization remains a useful diagnostic tool of aromaticity for many authors.[9] Such a current should manifest itself in the values and signs of all magnetic properties of the compound, especially as a large negative contribution to the out-of-plane component of the magnetic susceptibility, which is precisely what is observed.[10]

Arguably, magnetic properties are the most heterogeneous group of aromaticity characteristics, not only because numerous properties have been used but also because of the different means by which they are calculated or measured. At present, the magnetic values used for aromaticity investigations are more and more frequently calculated rather than measured. Moreover, some of them, such as ring current, are not observable quantities. Apart from a variety of magnetic effects there is also a diversity of methods for their calculation. For example, NICS (nuclear independent chemical shift) can be calculated by the GIAO (gauge-independent atomic orbital) method (as in the original method of Schleyer *et al.*[11]), but it also can be calculated by means of others, such as individual gauges for atoms in molecules, IGAIM methods.

Occasionally, some authors claim a particular magnetic parameter to be superior to others in representing the aromaticity of compounds. For instance, calculated chemical NMR shifts were considered to be such reliable parameters, as they can be measured with high accuracy in NMR spectroscopy and calculated shifts are in good agreement with experiment.[12] Magnetic susceptibility exaltation Λ, the difference between the magnetic susceptibility of a cyclic conjugated system and that of a hypothetical cyclic system with localized double bonds in which the ring current vanishes, is yet another parameter which once was considered to be the only uniquely applicable aromaticity criterion[13–15]—aromatic compounds are characterized by significantly enhanced diamagnetic susceptibility.

Flygare and co-workers advocated the utilization of diamagnetic anisotropy, χ_{aniso}, and the susceptibility component perpendicular to the ring plane, χ_{zz}.[16,17] However, it has been pointed out that electron delocalization influences only the out-of-plane component of the susceptibility and that the local and non-local contributions to χ_{aniso} must be differentiated between and only the latter can constitute aromaticity indices.[10,18] A quantitative measure of electron delocalization in a planar, cyclic

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molecule may be obtained by comparing the measured out-of-plane magnetizability component or magnetic anisotropy with the value predicted for a hypothetical structure in which the electron distribution is completely localized. The difference between the observed and calculated values, $\Delta\chi_{ani}$ and $\Delta\chi_{zz}$, is the estimate of the extent of electron delocalization and of the relative aromaticity. Currently, the enhancement of magnetic susceptibility, Λ, has been calculated by comparing corresponding susceptibilities of the reagents of corresponding homodesmotic reactions, and so have $\Delta\chi_{ani}$ and $\Delta\chi_{zz}$.

Recently, the NICS is the calculated magnetic property of rings that some authors consider to be better than others.[19,20] However, this parameter has also been criticized,[9,21] on the ground that its physical meaning is not clear at all.

The mutual relationships between the magnetic and other (structural and energetic) aromaticity parameters have been thoroughly discussed, with special attention being given to whether any linear relationship exists between them. It has been observed that these relationships depend heavily on the selection of molecules in the sample. They may also depend on the choice of indices in the set.[3] In what follows, it is hardly unexpected that different authors should express different opinions on this point. One hint is that using three magnetic characteristics, Katritzky and co-workers found that two of them, χ_m (experimental molar susceptibility) and Λ (diamagnetic susceptibility exaltation), were almost completely orthogonal (uncorrelated) to the parameters of classical aromaticity, such as Bird's I_5[22] and I_6,[23] and they even postulated two types of aromaticity, which were designated 'classical' and 'magnetic'.[2,24,25] On the other hand, Jug and Köster[26] used different parameters for another set of compounds and stated that aromaticity is an at least two-dimensional phenomenon, but did not obtain the same orthogonality as Katrizky *et al.*[2]

Nevertheless, there have been various reports on better or worse linear relationships between some magnetic and some other (classical) indices.[13,27,28]

It would be relevant to ask what the mutual relations between the magnetic indices themselves are. Whereas appreciable attention has been paid to the problem of the relations between the magnetic and other ('classical') aromaticity parameters,[2,13,19,24–28] the associations between the magnetic properties themselves have not yet been thoroughly explored. In one approach, the authors compared correlation coefficients for Λ and NICS and NICS(1) (nuclear independent magnetic shift in the ring center and 1 Å above the center, respectively) for a large group of five-membered heterocycles[19] [with aromatic stabilization energy, ASE, larger than $5\,kcal\,mol^{-1}$ ($1\,kcal = 4.184\,kJ$)]. The authors claimed that for the set no good correlation can be obtained. However, some of their correlation coefficients are high, taking into consideration that numerous samples were used: $n = 27$ or 66. The correlation coefficient is a measure of the linear correlation between two variables. 'Goodness' of correlation can be measured as a probability that the association is statistically significant (and not occurring by chance, e.g. by the particular representation of the whole population). For $n = 66$, the critical value of the correlation (r) coefficient at the probability level $P = 1\%$ is 0.315. Any r value higher than 0.315 is statistically significant with a probability $> 99\%$.[29] In this regard, association of Λ with NICS is significant at that level, that of NICS with NICS(1) is highly significant but the correlation of Λ with NICS(1) is far less significant with probability at the level of 10% only.

Here, we compare greater number of magnetic characteristics for three groups of aromatic compounds:

1. five-membered unsubstituted heterocyclics, $n = 15$, differing in type or number of heteroatoms in the ring;
2. 2*H*-tetrazole derivatives, differing in type of substituent at C5, and possessing the same CN4 five-membered ring, $n = 15$;
3. six-membered unsubstituted heterocycles, $n = 12$.

We are also concerned with the mutual relationships between magnetic and other aromaticity indices. We will present the results numerically, through tables of correlation coefficients.

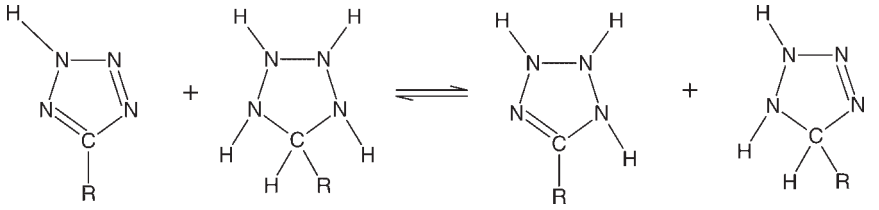
CALCULATIONS

There are many methods of calculating magnetic properties, which differ especially with respect to the gauge origin of the vector potential of the magnetic field. The method selected for calculating NICS values was the GIAO method (gauge-independent atomic orbital),[30] since it was used for this purpose in the original paper.[11] Other magnetic properties have been calculated using the IGAIM (individual gauges of atoms in molecules)[31] method. The results were almost the same as those obtained with the CSGT (continuous set of gauges transformation) method. The IGAIM and CSGT methods have been routinely used for the calculation of magnetic properties,[19,20,32,33] except NICSs.

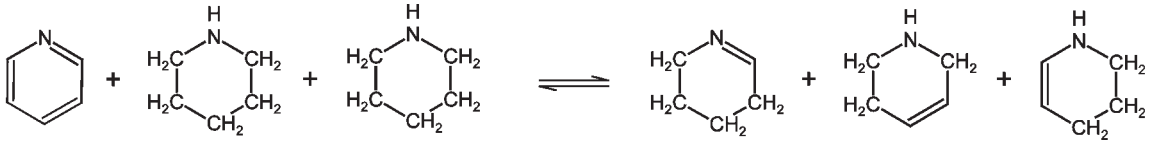
The above-mentioned GIAO and IGAIM methods have been implemented in Gausian 98[34] and all calculations were performed using this program. The geometry optimization and magnetic properties were calculated at the B3LYP/6–311++G** level. Many parameters which were calculated during this work had been reported previously, e.g. data for various five-membered heterocycles.[19] We recalculated them once again in order to have all the parameters needed for the compounds of the three groups obtained by the same method and at the same level. This was necessary for making comparisons between the groups.

The magnetic characteristics calculated for each group are the following: susceptibility, χ_{iso}, equalling $1/3(\chi_{11} + \chi_{22} + \chi_{33})$, where χ_{nn} are elements of the

magnetic susceptibility tensor; anisotropy of the susceptibility tensor, equalling the out-of-plane minus the average in plane magnetic susceptibility tensor components, χ_{aniso}, and the component of magnetic susceptibility perpendicular to the ring plane, χ_{zz}, in addition to NICS and NICS(1). To these parameters we added three other 'excess' parameters based on the homodesmotic reactions: Λ, $\Delta\chi_{ani}$ and $\Delta\chi_{zz}$. The last three were derived from the comparison of χ_{iso}, χ_{ani} and χ_{zz} for the compounds in the set with those calculated for the localized structures in which the ring current vanishes. For five-membered heterocycles, the excess values were calculated according to the same reaction scheme which was used previously:[6,35]



For the six-membered heteroaromatics, the excess values were calculated according to the scheme taking pyridine as an example:



In the case when the two possibilities of the arrangement of single and double bonds in a molecule resulted in different reaction schemes (pyridazine, 1,2,4-triazine, 1,2,3,4-tetrazine), the mean of the two calculated excess values was taken. However, the results of these calculations cannot be fully satisfactory because the rings of the reaction species are planar only in a rough approximation, so the in-plane and out-of-plane components of magnetic susceptibility have only an approximate meaning.

One more parameter, the ^{1}H NMR chemical shift (δ^1H), was added to the group of substituted tetrazoles as it is known to be very useful for studying aromatic character.[36] However, this parameter was not introduced for the other two subgroups because local anisotropic effects can substantially affect proton shielding[37] and therefore the protons to be compared must be located in similar regions of the magnetic field.[38] That is why we calculated the δ^1H values only for the subgroup where the proton is attached to the same (N) atom of the same ring.

RESULTS

Magnetic parameters for the three groups of compounds are suggested in Tables 1–3. It has been shown that only non-local contributions to χ^{iso}, χ_{aniso} and χ_{zz} can function as aromaticity indices,[10,18,39] and these three values are given for comparison purposes. For the sign of Λ, the convention is accepted that for aromatic molecules $\Lambda > 0$.[15,40] Consequently, the same convention was adopted for two other excess properties, $\Delta\chi_{aniso}$ and $\Delta\chi_{zz}$. For NICSs the signs of the computed values are reversed to correspond with the familiar NMR chemical shift convention,[11] hence negative NICSs denote aromaticity. In principle, the analysis was restricted to aromatic compounds, i.e. those which exhibit significant (larger than 3 ppm) enhancement of magnetic susceptibility—this is a criterion which responds uniquely to the presence of appreciable π electron delocalization in molecules.[15] However, in Table 3, one exception, 1,2-oxazine, is given to show which magnetic parameters differ in their signs or/and size when this compound is compared with the others considered aromatic. 1,2-oxazine, unlike the rest, cannot be regarded as an aromatic compound as its parameters (except for χ_{iso}) depart from those for the other compounds.

Tables 4–6 show correlations between the magnetic parameters within each of the groups. As can be seen, the correlations for each group are different. We are mainly interested here in the correlations having a significance level $<1\%$. Statistically this means that only one in 100 of these will be significant purely by chance.[41] The correlation with that significance level can be safely regarded as indicating a systematic relation. For the group of different five-membered heterocycles, the closest correlation was found between χ_{iso} and χ_{zz} and between $\Delta\chi_{aniso}$ and $\Delta\chi_{zz}$. Very significant correlations (significance level $<1\%$) were also found for eight other pairs (the corresponding entries are marked in bold).

Table 1. Calculated magnetic parameters of five-membered heterocycles: magnetic susceptibility χ_{iso}, anisotropy of magnetic susceptibility χ_{aniso}, the susceptibility component perpendicular to the ring plane, χ_{zz}, exaltation of the three parameters: Λ, $\Delta\chi_{aniso}$, and $\Delta\chi_{zz}$, and nuclear independent magnetic shift calculated at ring centers (NICS), and 1 Å above the ring centers, (NICS(1), in ppm

	χ_{iso}	Λ	χ_{aniso}	χ_{zz}	NICS	NICS(1)	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$
furan	−40.31	7.78	−39.69	−66.76	−11.92	−9.38	26.03	25.14
pyrrole	−45.21	11.23	−44.96	−75.18	−13.65	−10.09	33.61	33.64
thiophene	−53.04	10.49	−50.83	−86.93	−12.92	−10.28	33.78	33.01
tetrazole	−32.95	9.58	−49.52	−65.96	−14.47	−13.92	29.14	29.01
pyrazole	−40.70	11.70	−45.12	−70.78	−13.64	−11.34	30.41	31.97
imidazole	−40.78	10.21	−43.46	−69.75	−13.13	−10.58	30.55	30.58
oxazole	−36.69	6.49	−38.55	−62.39	−11.47	−9.74	24.83	23.04
isoxazole	−35.54	6.96	−40.62	−62.62	−12.29	−10.52	24.26	23.14
2,3-diazafuran	−31.42	7.11	−42.96	−60.06	−13.74	−11.64	25.89	24.37
2,5-diazafuran	−30.84	4.50	−45.00	−60.84	−13.46	−12.33	21.08	18.56
2,4-diazafuran	−32.87	6.35	−38.88	−58.79	−11.88	−10.67	26.75	24.19
3,4-diazafuran	−33.16	6.61	−39.00	−59.16	−11.13	−10.30	32.91	28.54
2,5-diazapyrrole	−36.63	10.17	−46.95	−67.93	−13.98	−12.79	23.39	25.76
2,4-diazapyrrole	−37.27	10.60	−43.51	−66.28	−13.09	−11.59	32.58	32.32
3,4-diazatiophene	−43.81	10.36	−52.25	−78.64	−13.66	−12.23	46.44	41.31

Table 2. Calculated magnetic parameters of tetrazole derivatives: magnetic susceptibility, χ_{iso}, anisotropy of magnetic susceptibility, χ_{aniso}, the susceptibility component perpendicular to the ring plane, χ_{zz}, exaltation of the three parameters: Λ, $\Delta\chi_{aniso}$, and $\Delta\chi_{zz}$, ^{1}H magnetic shift, δ^1H, and nuclear independent magnetic shift calculated at ring centers, NICS and 1 Å above the ring centers, NICS(1), in ppm

	χ_{iso}	Λ	χ_{aniso}	χ_{zz}	NICS	NICS1	$\delta\ ^1$H	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$
R									
BH2	−33.52	18.41	−65.17	−76.97	−13.43	−13.93	12.46	16.35	29.34
H	−32.95	10.24	−49.51	−65.96	−14.47	−13.92	12.10	25.16	27.01
OCH3	−46.70	9.00	−38.17	−72.15	−12.68	−11.95	11.28	26.26	26.51
Br	−57.99	7.44	−40.62	−85.07	−10.91	−4.76	11.96	35.50	31.11
Cl	−49.08	6.64	−41.63	−76.84	−13.16	−12.69	11.83	32.07	29.36
CH3	−42.94	9.54	−44.85	−72.84	−13.34	−13.32	11.74	21.75	23.98
CN	−41.37	9.72	−42.17	−69.48	−14.54	−13.77	12.10	25.80	26.92
NH2	−40.19	7.49	−36.54	−64.55	−12.21	−11.62	11.19	19.97	20.80
F	−36.69	6.47	−39.66	−63.13	−13.37	−12.27	11.45	24.95	24.21
NO2	−38.84	7.83	−58.42	−77.79	−13.76	−13.20	12.03	25.46	24.80
CF3	−55.05	10.13	−47.67	−86.83	−14.03	−13.71	12.05	27.43	28.41
CHO	−35.47	10.57	−58.39	−74.40	−13.62	−13.65	12.22	26.48	28.22
SiH3	−45.27	9.16	−49.53	−78.29	−14.19	−14.10	12.18	22.48	24.14
N_3	−47.09	8.76	−36.02	−71.11	−12.68	−12.15	11.61	45.38	39.01
$N(CH_3)_2$	−59.41	9.37	−37.44	−84.37	−11.92	−11.59	11.19	*	*

* These values for $N(CH_3)_2$-tetrazole could not be calculated.

Similar results for the second group of compounds, the substituted tetrazoles, are displayed in Table 5. It can be seen that in this case the relations between variables are different. Among the magnetic parameters, a close correlation was found for five pairs only: between χ_{zz} and χ_{iso}, between χ_{aniso} and Λ, between χ_{aniso} and δ^1H and between NICS and NICS(1), $\Delta\chi_{aniso}$ and $\Delta\chi_{zz}$.

Data for the third group are given in Tables 6 and 7. For the calculation of the correlations displayed in Table 6, only 11 compounds which can be regarded as aromatics were taken. In this case, there are six pairs of closely related parameters. Four of these are the same as in Table 4 for five-memebered heterocycles. The correlation coefficients between magnetic parameters for all 12 compounds are reported in Table 7. It can be seen that the coefficients in Table 7 (for $n = 12$) are generally much higher than those in Table 6 (for $n = 11$). The number of significant correlations (according to the currently accepted criterion) increased from six to 20.

In view of such different pictures of the relations between magnetic indices, we wanted to see whether the correlations between the magnetic characteristics and other aromaticity indices would be more similar when comparing the three groups. The structural parameters that we selected were the following: HOMA,[42] I_5,[22] I_6[23] and a minimum bond order in the ring, BO_{min};[43] as the electronic parameters, LP[5] and SDn;[6] and as energetic, the aromatic stabilization energy, ASE,[35] calculated with the use of the homodesmotic reaction given in Eqn (1). Details concerning the indices are not summarized here

Table 3. Calculated magnetic parameters of six-membered heterocycles: magnetic susceptibility χ_{iso}, anisotropy of magnetic susceptibility χ_{aniso}, the susceptibility component perpendicular to the ring plane, χ_{zz}, exaltations of the three characteristics: Λ, $\Delta\chi_{aniso}$, and $\Delta\chi_{zz}$, and nuclear independent magnetic shift calculated at ring centers, (NICS), and 1 Å above the ring centers (NICS(1), in ppm

	χ iso	Λ	χ_{aniso}	χ_{zz}	NICS	NICS1	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$
1,2-oxazine	−38.66	0.09	−4.39	−41.59	1.10	1.28	−7.02	−4.59
pyridone	−46.66	4.44	−33.53	−69.02	−2.42	−4.25	14.99	14.43
1,2,3-triazine	−33.39	8.06	−63.82	−75.94	−4.32	−10.83	36.63	32.48
s-triazine	−37.48	3.71	−52.70	−72.61	−4.06	−9.67	20.80	17.57
1,2,4-triazine	−34.18	8.30	−60.89	−74.77	−3.78	−10.37	29.43	27.92
pentazine	−22.89	3.75	−61.29	−63.75	−0.63	−10.65	28.88	23.00
1,2,4,5-tetrazine	−28.06	6.33	−62.16	−69.50	−1.83	−10.60	26.90	24.27
pyrimidine	−41.40	10.69	−58.44	−80.36	−5.52	−10.02	32.24	32.18
pyridazine	−39.26	10.40	−64.50	−82.26	−5.35	−10.54	51.93	45.02
pyrazine	−40.47	12.56	−61.37	−81.39	−5.33	−10.26	34.36	35.47
pyridine	−46.50	12.26	−63.48	−88.82	−6.80	−18.62	38.53	37.95
1,2,3,4-tetrazine	−27.83	8.98	−62.79	−69.69	−2.69	−10.81	30.11	29.05

Table 4. Correlation coeffifcients[a] (top rows) between magnetic indices[b] of five-membered heterocycles (n = 15), and their significance levels (bottom rows, italics)

	χ_{iso}	Λ	χ_{aniso}	χ_{zz}	NICS	NICS(1)	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$
χ_{iso}	1.0							
Λ	**−0.68**	1.0						
	(0.006)							
χ_{aniso}	0.49	−0.59	1.0					
	(0.062)	*(0.019)*						
χ_{zz}	**0.95**	**−0.74**	**0.75**	1.0				
	(0.000)	***(0.002)***	***(0.001)***					
NICS	0.10	−0.54	**0.77**	0.36	1.0			
	(0.722)	*(0.039)*	***(0.001)***	*(0.184)*				
NICS(1)	−0.36	−0.16	0.61	−0.05	**0.77**	1.0		
	(0.192)	*(0.586)*	*(0.015)*	*(0.870)*	***(0.001)***			
$\Delta\chi_{aniso}$	−0.57	0.57	−0.53	−0.63	−0.15	−0.03	1.0	
	(0.027)	*(0.026)*	*(0.041)*	*(0.011)*	*(0.598)*	*(0.926)*		
$\Delta\chi_{zz}$	**−0.68**	**0.80**	−0.62	**−0.75**	−0.32	−0.08	**0.95**	1.0
	(0.006)	***(0.000)***	*(0.014)*	***(0.001)***	*(0.249)*	*(0.780)*	***(0.000)***	

[a] Magnetic indices are the same as those in Table 1.
[b] The entries corresponding to the close correlations are given in bold.

because this task has been performed extensively in several accounts in the special issue of *Chemical Reviews* (May 2001) devoted to aromaticity.

Correlations between the magnetic indices and the others are given in Tables 8–10. For the first group of different five-membered heterocyclic compounds there are 13 pairs of closely correlated indices. Λ is the magnetic parameter which is best correlated with three structural and two electronic indices; a few correlations were also found for χ_{aniso} and NICS (Table 8). The close correlation of Λ with HOMA and much weaker with NICS for this group (Table 4) is in agreement with the previous results.[19]

The data in Table 9 illustrate that for the tetrazole derivatives, Λ is well correlated with two structural parameters, I_5 and BO_{min}, and with ASE, δ^1H with both electronic parameters LP and SDN, and χ_{aniso} with LP. In this case, HOMA can be considered to be 'orthogonal' to all the magnetic indices.

Comparison of the data in Tables 4 and 8 on the one hand with those in Tables 5 and 9 on the other shows that there are more significantly correlated pairs for the first group of compounds (Tables 4 and 8) than for the second group (Tables 5 and 9), in spite of Tables 5 and 9 having more entries than Tables 4 and 8. This suggests that for the compounds differing in substituents on the same ring (second group), the aromaticity parameters are less correlated that for the first group of unsubstituted different five-membered rings.

The correlations presented in Table 10 for the six-memebered heterocycles ($n = 11$) are different once again—only three close correlations can be seen and in different pairs than for the other two groups. Here, the LP parameter is not given as it does not matter for the

Table 5. Correlation coefficients[a] (top rows) between magnetic indices[b] of tetrazole derivatives(n = 15) and their significance levels (bottom rows, italics)

	χ_{iso}	Λ	χ_{aniso}	χ_{zz}	NICS	NICS1	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$	δ^1H
χ_{iso}	1.00								
Λ	0.34	1.00							
	(0.208)								
χ_{aniso}	−0.54	**−0.67**	1.00						
	(0.039)	***(0.006)***							
χ_{zz}	**0.72**	−0.15	0.20	1.00					
	(0.002)	*(0.585)*	*(0.484)*						
NICS	−0.58	−0.26	0.49	−0.27	1.00				
	(0.024)	*(0.355)*	*(0.064)*	*(0.332)*					
NICS1	−0.55	−0.36	0.43	−0.30	**0.85**	1.00			
	(0.032)	*(0.185)*	*(0.114)*	*(0.284)*	***(0.000)***				
$\Delta\chi_{aniso}$	−0.55	−0.44	0.49	−0.18	0.38	0.44	1.00		
	(0.040)	*(0.118)*	*(0.078)*	*(0.527)*	*(0.179)*	*(0.117)*			
$\Delta\chi_{zz}$	−0.34	0.15	0.09	−0.30	0.24	0.24	**0.82**	1.00	
	(0.232)	*(0.597)*	*(0.762)*	*(0.306)*	*(0.417)*	*(0.417)*	***(0.000)***		
δ^1H	0.35	0.55	**−0.81**	−0.26	−0.56	−0.28	−0.18	0.19	1.00
	(0.200)	*(0.034)*	***(0.000)***	*(0.356)*	*(0.031)*	*(0.318)*	*(0.540)*	*(0.509)*	

[a] Magnetic indices are the same as those in Table 2.
[b] The entries corresponding to the close correlations are given in bold.

Table 6. Correlation coefficients[a] (top rows) between magnetic indices[b] for six-membered heterocycles (n = 11), and their significance levels (bottom rows, italics)

	χ_{iso}	Λ	χ_{aniso}	χ_{zz}	NICS	NICS1	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$
χ_{iso}	1.00							
Λ	−0.41	1.00						
	(0.208)							
χ_{aniso}	−0.45	−0.52	1.00					
	(0.167)	*(0.104)*						
χ_{zz}	0.69	**−0.85**	0.34	1.00				
	(0.019)	***(0.001)***	*(0.306)*					
NICS	0.72	**−0.80**	0.26	**0.97**	1.00			
	(0.012)	***(0.003)***	*(0.437)*	***(0.000)***				
NICS1	0.03	−0.54	0.70	0.60	0.51	1.00		
	(0.928)	*(0.083)*	*(0.016)*	*(0.050)*	*(0.109)*			
$\Delta\chi_{aniso}$	−0.05	0.69	−0.74	−0.65	−0.56	−0.54	1.00	
	(0.881)	*(0.018)*	*(0.010)*	*(0.030)*	*(0.070)*	*(0.085)*		
$\Delta\ \chi_{zz}$	−0.19	**0.86**	−0.71	**−0.77**	−0.69	−0.58	**0.97**	1.00
	(0.585)	***(0.001)***	*(0.014)*	***(0.005)***	*(0.019)*	*(0.059)*	***(0.000)***	

[a] Magnetic indices are the same as those in Table 3.
[b] The entries corresponding to the close correlations are given in bold.

aromatic properties of the compounds in the group. In Table 10, the ASE values were also omitted. They were calculated according to Eqn (2), similarly to the 'excess' magnetic properties. However, their values were inconsistent: some of the values were positive whereas others were negative. What is more, when two possible arrangements of single and double bonds in a molecule were possible (pyridazine, 1,2,4-triazine, 1,2,3,4-tetrazine), one of the values could be positive and the second negative. We suppose that in this case, some extraneous factors, such as strains, differences in planarity and minor hybridization differences, could influence the energies of the reagents and that the ASE calculated in such a way does not uniquely represent the true aromatic stabilization energy. For the five-membered heteroaromatics the ASE values seem to be correct (all values are positive) but they also have to be treated with caution. On the other hand, the magnetic excess values thus calculated are probably less influenced by the structural effects because it has been shown that the diamagnetic susceptibility tensor is relatively insensitive to the bonding in the molecule.[18]

When the same correlations as in Table 10 were calculated for 12 compounds (including 1,2-oxazine) (the data are not given here), the number of significant correlations increased from 3 to 13.

An explanation of the effect of improving the correlations on addition of a compound that is an 'outlier' with respect to the set, or on combining two different groups in the set, can be found on the basis of statistics. To calculate

Table 7. Correlation coefficients[a] (top rows) between magnetic indices[b] for six-membered heterocycles (n = 12), and significance levels (bottom rows, italics)

	χ_{iso}	Λ	χ_{aniso}	χ_{zz}	NICS	NICS1	$\Delta\chi_{aniso}$	$\Delta\chi_{zz}$
χ_{iso}	1.00							
Λ	−0.27	1.00						
	(0.396)							
χ_{aniso}	−0.30	**−0.73**	1.00					
	(0.347)	***(0.008)***						
χ_{zz}	0.32	**−0.89**	**0.81**	1.00				
	(0.307)	***(0.000)***	***(0.001)***					
NICS	0.50	**−0.87**	0.65	**0.95**	1.00			
	(0.101)	***(0.000)***	*(0.021)*	***(0.000)***				
NICS1	−0.05	**−0.74**	**0.88**	**0.84**	**0.73**	1.00		
	(0.875)	***(0.006)***	***(0.000)***	***(0.001)***	***(0.006)***			
$\Delta\chi_{aniso}$	0.04	**0.82**	**−0.90**	**−0.87**	**−0.77**	**−0.80**	1.00	
	(0.898)	***(0.001)***	***(0.000)***	***(0.000)***	***(0.004)***	***(0.001)***		
$\Delta\chi_{zz}$	−0.05	**0.90**	**−0.88**	**−0.91**	**−0.83**	**−0.82**	**0.98**	1.00
	(0.878)	***(0.000)***	***(0.000)***	***(0.000)***	***(0.001)***	***(0.001)***	***(0.000)***	

[a] Magnetic indices are the same as those in Table 3.
[b] The entries corresponding to the close correlations are given in bold.

Table 8. Correlation coefficients[a] (top rows) between magnetic,[b] structural (HOMA, I_5, BOmin), electronic (LP, SDN), and energetic (ASE) indices of five-membered heterocycles (n = 15) and their significance levels (bottom rows, italics)

	HOMA	I_5	BOmin	LP	SDN	ASE
χ_{iso}	−0.33	−0.20	−0.41	−0.24	0.39	0.05
	(0.237)	*(0.468)*	*(0.133)*	*(0.394)*	*(0.146)*	*(0.866)*
Λ	**0.75**	**0.71**	**0.74**	**0.80**	**−0.83**	0.5
	(0.001)	***(0.003)***	***(0.002)***	***(0.000)***	***(0.000)***	*(0.059)*
χ_{aniso}	**−0.65**	−0.54	−0.51	**−0.68**	**0.76**	−0.32
	(0.009)	*(0.040)*	*(0.050)*	***(0.005)***	***(0.001)***	*(0.240)*
χ_{zz}	−0.49	−0.35	−0.50	−0.43	0.58	−0.08
	(0.065)	*(0.196)*	*(0.057)*	*(0.107)*	*(0.022)*	*(0.769)*
NICS	**−0.72**	−0.61	−0.43	**−0.76**	**0.81**	**−0.70**
	(0.002)	*(0.017)*	*(0.111)*	***(0.001)***	***(0.000)***	***(0.003)***
NICS(1)	−0.54	−0.56	−0.33	**−0.65**	0.56	−0.51
	(0.038)	*(0.029)*	*(0.223)*	***(0.009)***	*(0.029)*	*(0.050)*
$\Delta\chi_{aniso}$	0.23	0.15	0.29	0.31	−0.33	−0.24
	(0.404)	*(0.593)*	*(0.299)*	*(0.254)*	*(0.226)*	*(0.389)*
$\Delta\chi_{zz}$	0.46	0.38	0.50	0.54	−0.56	0.02
	(0.083)	*(0.157)*	*(0.060)*	*(0.037)*	*(0.028)*	*(0.942)*

[a] Magnetic indices are the same as those in Table 1.
[b] The entries corresponding to the close correlations are given in bold.

the correlations when the sample comprises different subgroups may be misleading: mixing them tends to inflate the correlation.[44] Here, addition of only one non-aromatic compound to 11 aromatic compounds efficiently improves most of the correlations. The effect can probably provide an explanation for the finding reported in Ref. 19, namely that correlations for a large set of five-membered π compounds the aromaticity criteria were larger when the whole set of compounds was introduced than in the case when comparisons were restricted to some groups of compounds, e.g. aromatic compounds with ASE $>5\,\mathrm{kcal\,mol^{-1}}$. However, contrary to the authors' conclusion, the correlations inside the aromatic subgroups are significant for eight pairs (out of 10) at a significance level of 1%.

In the present investigation there are more close correlations in the groups of unsubstituted five- and six-membered rings than in the group including different substituted derivatives to the same ring. This was observed for magnetic vs magnetic and magnetic vs 'classical' indices and also within the sets of 'classical' (structural and electronic) indices, for which the relevant correlations coefficients are not reported here.

The picture which emerges from our investigation is complex. The analysis clearly shows that the relations between aromaticity indices depend on the choice of the

Table 9. Correlation coefficients[a] (top rows) between magnetic,[b] structural (HOMA, I_5, BO_{min}), electronic (LP, SDN), and energetic (ASE) indices of tetrazole derivatives (n = 15), and their significance levels (bottom rows, italics)

	HOMA	I_5	BOmin	LP	SDN	ASE
χ_{iso}	0.29	−0.11	0.08	0.42	−0.07	0.32
	(0.287)	*(0.707)*	*(0.770)*	*(0.120)*	*(0.812)*	*(0.240)*
Λ	−0.38	**−0.83**	**−0.65**	0.41	−0.13	**0.72**
	(0.157)	***(0.000)***	***(0.009)***	*(0.133)*	*(0.653)*	***(0.002)***
χ_{aniso}	0.00	0.44	0.18	**−0.75**	0.50	−0.51
	(1.000)	*(0.099)*	*(0.528)*	***(0.001)***	*(0.056)*	*(0.053)*
χ_{zz}	0.34	0.24	0.24	−0.13	0.33	−0.04
	(0.211)	*(0.389)*	*(0.386)*	*(0.640)*	*(0.223)*	*(0.883)*
NICS	−0.30	0.009	−0.09	−0.55	0.32	−0.372
	(0.274)	*(0.975)*	*(0.745)*	*(0.034)*	*(0.247)*	*(0.173)*
NICS(1)	0.02	0.27	0.18	−0.30	0.00	−0.34
	(0.936)	*(0.337)*	*(0.510)*	*(0.271)*	*(0.998)*	*(0.219)*
$\Delta\chi_{aniso}$	0.55	0.52	0.40	−0.06	−0.28	−0.15
	(0.040)	*(0.054)*	*(0.156)*	*(0.841)*	*(0.336)*	*(0.617)*
$\Delta\chi_{zz}$	0.05	0.01	−0.02	0.23	−0.41	0.34
	(0.858)	*(0.981)*	*(0.939)*	*(0.437)*	*(0.147)*	*(0.238)*
δ ^{1}H	0.26	−0.23	−0.07	**0.88**	**−0.79**	0.60
	(0.352)	*(0.410)*	*(0.803)*	***(0.000)***	***(0.000)***	*(0.019)*

[a] Magnetic indices are the same as those in Table 2.
[b] The entries corresponding to the close correlations are given in bold.

indices and of the corresponding molecules, as has already been mentioned, and that with the set of parameters chosen in the present work no general rules can be found. However, many significant correlations exist between different indices.

It can be seen not only that the 'classical' aromaticity indices can be orthogonal to the magnetic ones, but also that some magnetic parameters themselves may be orthogonal to others (and mostly are).

The lack of a close correlation for many pairs of magnetic indices suggests that ring current cannot be the unique physical nature of aromatic stabilization. Were it so, the magnetic properties, at least the excess ones ($\Lambda = \Delta\chi_{iso}$, $\Delta\chi_{aniso}$, $\Delta\chi_{zz}$) and perhaps the ^{1}H chemical shift should be more related to each other.

Table 10. Correlation coefficients[a] (top rows) between magnetic,[b] structural (HOMA, I_5, BO_{min}), and electronic (SDN) indices of six-membered heterocycles (n = 11) and significance levels (bottom rows, italics)

	HOMA	I_6	BOmin	SDN
χ_{iso}	0.40	0.63	0.34	−0.56
	(0.218)	*(0.037)*	*(0.309)*	*(0.075)*
Λ	0.38	0.05	0.36	0.32
	(0.248)	*(0.876)*	*(0.270)*	*(0.343)*
χ_{aniso}	**−0.91**	**−0.77**	**−0.85**	0.03
	(0.000)	***(0.006)***	***(0.001)***	*(0.935)*
χ_{zz}	−0.31	0.04	−0.33	−0.56
	(0.348)	*(0.906)*	*(0.315)*	*(0.071)*
NICS	−0.30	0.06	−0.32	−0.50
	(0.375)	*(0.872)*	*(0.331)*	*(0.116)*
NICS(1)	−0.65	−0.52	−0.66	−0.69
	(0.029)	*(0.105)*	*(0.028)*	*(0.020)*
$\Delta\chi_{aniso}$	0.54	0.25	0.47	0.09
	(0.084)	*(0.462)*	*(0.144)*	*(0.793)*
$\Delta\chi_{zz}$	0.53	0.20	0.47	0.18
	(0.096)	*(0.563)*	*(0.146)*	*(0.600)*

[a] Magnetic indices are the same as those in Table 3.
[b] The entries corresponding to the close correlations are given in bold.

CONCLUSIONS

The analysis made here for sets comprising solely magnetic characteristics revealed that there exist many pairs of parameters orthogonal to each other within the pair; there exist also a few pairs of the characteristics correlated within a pair (Tables 4–6). That is why for a given sample of compounds, some magnetic parameters can be orthogonal to the rest of the aromaticity indices, whereas others can correlate with them to a greater or smaller extent (Tables 8–10). The data in Tables 4–10 show that the correlations are different for the three sets of compounds investigated here. The correlations can be inflated when the objects belonging to different subgroups (e.g. aromatic and non-aromatic ones) are combined in a set. The results suggest that the properties calculated here cannot be thoroughly accounted for by the corresponding ring currents, and that other effects, despite the lack of satisfactory identification yet,[4] have also intruded upon the properties being calculated.

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