

## Aromaticity as a Quantitative Concept. 7. Aromaticity Reaffirmed as a Multidimensional Characteristic<sup>†</sup>

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Recent claims that linear relationships exist between energetic, geometric, and magnetic criteria of aromaticity are shown to be invalid for any representative set of heteroaromatics in which the number of heteroatoms varies.

The concept of aromaticity is of central importance to the theory and practice of teaching and research in organic chemistry. Among carbocyclic compounds, the aromatic derivatives form an extremely important class, and their reactivity, stability, and physical properties are profoundly influenced by their aromatic character. The concept of aromaticity is of even greater importance in heterocyclic chemistry. The large majority of known compounds are heterocyclic, and heterocycles form the basis of life and are seminal in technology and medicine. All serious treatments of heterocyclic chemistry, from the most advanced<sup>1</sup> to the more elementary,<sup>2</sup> rely heavily on the concept of aromaticity—not only as a qualitative but also as a quantitative measure. Thus it is universally agreed that, for example, pyridine is more aromatic than furan. It would be inconceivable to discontinue the use of the concept of aromaticity because of difficulties in its definition and/or measurement.

In view of the basic importance of aromaticity, it is unsurprising that many scales of aromaticity have been proposed and that there have been many attempts to unite these into one universally applicable quantitative measure of aromaticity. Within restricted classes of compounds, significant progress has been made in this direction—a good example being the Hückel annulenes.<sup>3</sup> However, over a wider variety of structures, and particularly when heterocyclic compounds are included, strong evidence has been advanced that quantitatively aromaticity is a multidimensional characteristic. In the first paper of this series,<sup>4a</sup> one of our groups demonstrated that at least two principal components, identified with

“classical” and “magnetic” aromaticity, were required to describe a set of 12 common quantitative aromaticity criteria. These criteria were originally derived from 9 compounds,<sup>4a</sup> and later extended<sup>4a–d</sup> to a total of 59 mono- and bicyclics. This evidence for the multidimensionality of aromaticity was later supported by independent evidence from the groups of two more of the present authors. By the application of factor analysis to five different models defining aromaticity indices,<sup>5a</sup> Krygowski concluded that even for a homologous sample of 22 benzenoid hydrocarbons two independent factors are necessary to describe the total variance; he found similar results for a variety of other cases.<sup>5b–g</sup> Jug’s paper<sup>6</sup> demonstrated that there is no absolute assessment of an orthogonality of geometric, energetic, and magnetic criteria, but in general aromaticity was shown to be at least two-dimensional, independently of the level of the computational method employed.

We consider it important to reaffirm the multidimensionality of aromaticity in the light of recent denials by the Schleyer group<sup>7</sup> and by Bird.<sup>8</sup> Schleyer claimed<sup>7</sup> to have demonstrated that “linear relationships exist among the energetic, geometric and magnetic criteria of aromaticity and that these relationships even extend to anti-aromatic systems”.<sup>9</sup> Bird claimed<sup>8</sup> that good linear relationships exist between experimental diamagnetic susceptibility enhancements and the corresponding resonance energies and/or aromaticity indices for some 50 aromatic and heteroaromatic ring systems. Both groups concluded they had demonstrated that there was no justification for separate “classical” and “magnetic” con-

<sup>†</sup> For part 6, see: Katritzky, A. R.; Karelson, M.; Wells, A. P. *J. Org. Chem.* **1996**, *61*, 1619.

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(1) See, for example: Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds. *Comprehensive Heterocyclic Chemistry II*; Elsevier: Oxford, 1996; Vols. 1–9.

(2) See, for example: Pozharzki, A. F.; Soldatenkov, A. T.; Katritzky, A. R. *Heterocycles in Life and Society*; John Wiley & Sons: Chichester, 1997.

(3) (a) Haddon, R. C. *J. Am. Chem. Soc.* **1978**, *100*, 1722. (b) Haddon, R. C.; Fukunaga, T. *Tetrahedron Lett.* **1980**, 1191.

(4) (a) Katritzky, A. R.; Barczynski, P.; Musumarra, G.; Pisano, D.; Szafran, M. *J. Am. Chem. Soc.* **1989**, *111*, 7. (b) Katritzky, A. R.; Feygelman, V.; Musumarra, G.; Barczynski, P.; Szafran, M. *J. Prakt. Chem.* **1990**, *332*, 853. (c) Katritzky, A. R.; Feygelman, V.; Musumarra, G.; Barczynski, P.; Szafran, M. *J. Prakt. Chem.* **1990**, *332*, 870. (d) Katritzky, A. R.; Barczynski, P. *J. Prakt. Chem.* **1990**, *332*, 885. (e) Katritzky, A. R.; Karelson, M.; Malhotra, N. *Heterocycles* **1991**, *32*, 127.

(5) (a) Krygowski, T. M.; Ciesielski, A.; Bird, C. W.; Kotschy, A. *J. Chem. Inf. Comput. Sci.* **1995**, *35*, 203. (b) Cyranski, M.; Krygowski, T. M. *Polish J. Chem.* **1995**, *69*, 1088. (c) Krygowski, T. M.; Cyranski, M. *Tetrahedron* **1996**, *52*, 1713. (d) Krygowski, T. M.; Cyranski, M. *Tetrahedron* **1996**, *52*, 10255. (e) Krygowski, T. M. *J. Chem. Inf. Comput. Sci.* **1993**, *33*, 70. (f) Krygowski, T. M.; Cyranski, M.; Ciesielski, A.; Swirska, B.; Leszczynski, P. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 1135. (g) Krygowski, T. M.; Wisiorowski, M.; Nakata, K.; Fujio, M.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2275.

(6) Jug, K.; Köster, A. M. *J. Phys. Org. Chem.* **1991**, *4*, 163.

(7) (a) Schleyer, P. von R.; Freeman, P. K.; Jiao, H.; Goldfuß, B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 337; (b) *Angew. Chem.* **1995**, *107*, 332. (c) Schleyer, P. von R.; Jiao, H. *Pure Appl. Chem.* **1996**, *68*, 209. (d) Subramanian, G.; Schleyer, P. von R.; Jiao, H. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2638. (e) However their latest paper<sup>3d</sup> shows a possible shift in their position as they concluded: “The quantitative relationship among the magnetic, energetic and geometric criteria of aromaticity has been demonstrated recently for a wide ranging set of five-membered heterocycles. However, we emphasize here that other influences are important.”

(8) Bird, C. W. *Tetrahedron* **1996**, *52*, 9945.

**Table 1.** ASE (kcal mol<sup>-1</sup>) and  $\Lambda$  (ppm cgs) Calculated Values for Some Aromatic and Heteroaromatic Compounds

Plot entry	Name	Structure	ASE [a]	$\Lambda$ [a]
1	phosphole		7.0 [b]	-3.3 [b]
2	silacyclopentadienyl anion		13.8 [b]	-7.7 [b]
3	furan		19.8 (19.8)	-9.1 (-9.1)
4	thiophene		22.4 (22.4)	-10.0 (-10.0)
5	pyrrole		25.5 (25.5)	-12.1 (-12.1)
6	cyclopentadienyl anion		28.8 (28.8)	-17.2 (-17.2)
7	benzene		26.7	-13.6
8	1H-1,2,4-triazole		26.2	-3.8
9	pentazole		10.8	-3.0
10	1,2,4-thiadiazole		19.1	-6.6
11	1,2,5-oxadiazole		26.4	-1.5
12	1,3,4-oxadiazole		14.9	-3.2
13	1,3,4-thiadiazole		13.3	-9.5

[a] Values from reference<sup>3a</sup> are in parentheses. [b] Values from reference.<sup>3a</sup>

cepts of aromaticity. Especially the papers by Schleyer have received considerable attention,<sup>10</sup> and their conclusions were repeated by Grützmacher<sup>11</sup> and Koch<sup>12</sup> in widely disseminated commentaries. As these conclusions<sup>7,8</sup> seemed in direct contradiction to those reached independently in three of our research groups,<sup>4-6</sup> we have carefully examined the evidence presented<sup>7,8</sup> that aromaticity is monodimensional.

In the final paper<sup>4d</sup> of the sequence by Katritzky, the scores plot for the first and second principal components for the complete set of 39 monocycles shows clearly that the number of heteroatoms is the dominant factor influencing the second principal component, but this number is much less important for the first component. The implication is that a linear relationship is ruled out for any representative set of heteroaromatics in which the number of heteroatoms varied. Indeed, this turns out to be the case. Table 1 shows the values of aromatic stabilization energy (ASE) and magnetic susceptibility exaltation  $\Lambda$  for benzene, cyclopentadienyl anion, and 11

(9) The supposedly equivalent German version<sup>3b</sup> went further, claiming one single relationship: "Unsere Arbeit zerstreut die pessimistische Schlußfolgerung von Katritzky et al., indem sie demonstriert, daß eine lineare Beziehung zwischen den energetischen, geometrischen und magnetischen Kriterien für Aromatizität besteht und daß sich dieser Zusammenhang sogar auf antiaromatische Systeme erstreckt." (An accurate translation of which is, "Our work dispels the pessimistic conclusion of Katritzky et al. in that it demonstrates that a linear relationship exists between the energetic, geometric and magnetic criteria of aromaticity and that this relationship even extends to antiaromatic systems.")

(10) Through 1996, ref 7a,b had been cited 41 times, ref 7c 8 times.

(11) (a) Grützmacher, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 295; (b) *Angew. Chem.* **1995**, *107*, 323.

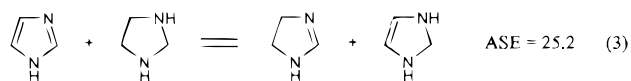
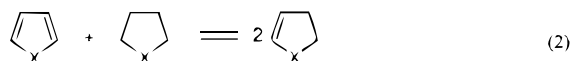
(12) Koch, W. *Nachr. Chem. Techn. Lab.* **1996**, *44*, 187.

heteroaromatic compounds. Typical six-membered rings are included for comparison. It has been claimed<sup>7c</sup> that the reason for nonlinearity in the early work was the use of poor data: we have attempted to lay this claim to rest. The data in Table 1 were calculated using the same methodology as reported in ref 7a. The geometries were calculated at ab initio level using 6-31G\* basis sets and the second-order Møller–Plesset perturbation theory within the frozen core approximation (6-31G\*/MP2(fc)). Gaussian 94 software was used for ab initio calculations.<sup>13</sup> The magnetic properties of molecules were calculated using the IGLO program<sup>14</sup> with the basis set II. The ab initio fixed geometries at the 6-31G\*/MP2(fc) level were used in IGLO calculations.

The magnetic susceptibility exaltation,  $\Lambda$ , is defined by eq 1 as the difference between the magnetic susceptibilities of an aromatic compound ( $\chi_M$ ) and a corresponding hypothetical analogue lacking cyclic delocalization ( $\chi'_M$ ).

$$\Lambda = \chi_M - \chi'_M \quad (1)$$

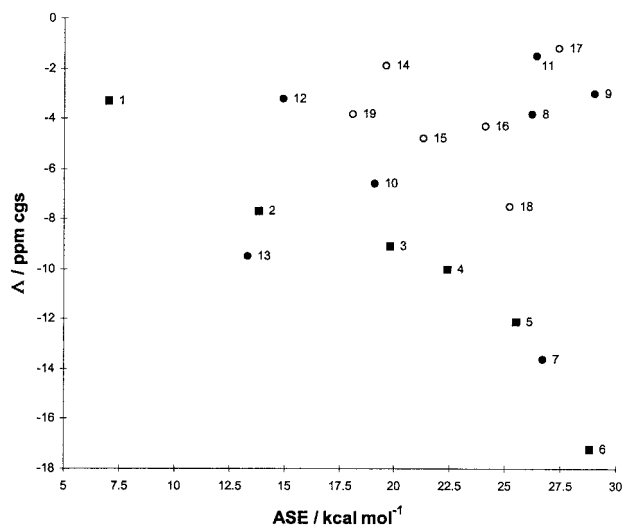
We calculated magnetic susceptibilities for these non-aromatic models using the additive scheme devised and used by Schleyer's group.<sup>7a</sup> The following structural increments used for estimating  $\Lambda$ :  $-\text{CH}=\text{}$ ,  $>\text{CH}-$ ,  $>\text{S}$ ,  $>\text{SiH}-$ ,  $>\text{O}$ ,  $>\text{PH}$ , and  $>\text{NH}$  are  $-9.1$ ,  $+2.2$ ,  $-20.3$ ,  $-19.93$ ,  $-3.8$ ,  $-21.0$ , and  $-8.0$ , respectively.<sup>7a</sup> Since the increment value for  $-\text{N}=\text{}$  was not listed by Schleyer, we derived the value  $-7.7$  using the same methodology as reported in ref 7a. Again following ref 7a, ASE is calculated as the energetic effect of imaginary homodesmotic reaction (eq 2). However, the method used by Schleyer for estimating ASE values needs a modification to be rigorously defined for heteroaromatics with two (or more) different types of double bond (e.g.,  $-\text{C}=\text{C}-$  and  $-\text{C}=\text{N}-$ ). For example, ASE for imidazole is calculated by eq 3. The calculated ASE values are given in Table 2 together with the  $\Lambda$  values.



In Figure 1, we have taken that part of Figure 2 of ref 7a which corresponds to the practically and technically important familiar compounds included in Schleyer's work: phosphole, silacyclopentadienyl anion, furan, thiophene, and pyrrole. We have reproduced Schleyer's results for these same compounds as plotted in Figure 1. We have also plotted in Figure 1 our results from Tables 1 and 2 for a variety of other important heteroaromatics.

(13) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Peterson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Comperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94, Revision B.1*; Gaussian, Inc.: Pittsburgh, PA, 1995.

(14) VanWuellen, C.; Kutzelnigg, W. In *Methods and Techniques in Computational Chemistry: METECC-94*; Clementi, E., Ed.; STEF: Cagliari, 1993, Vol. B, Chapter 9.



**Figure 1.** Plot of the magnetic susceptibility exaltations  $\Delta$  versus ASE for some aromatic and heteroaromatic compounds,  $R^2 = 0.034$ : squares indicate compounds considered by Schleyer;<sup>3a</sup> solid circles indicate additional data with a single ASE value (see Table 1 for numerical designators of compound data points); open circles indicate data with alternative ASE values (see Table 2).

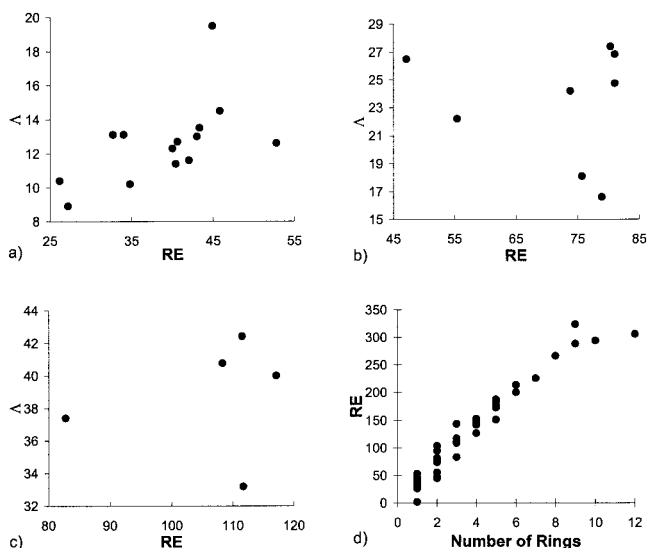
**Table 2.**  $\Delta$  (ppm cgs) and ASE (kcal mol<sup>-1</sup>) Calculated Values for Some Heteroaromatic Compounds with Two Different Types of Double Bond

Plot entry	Name	Structure	ASE	$\Delta$ [a]
14	pyrazine		19.6	-1.9
15	thiazole		21.3	-4.8
16	isoxazole		24.1	-4.3
17	1H-1,2,3,4-tetrazole		27.4	-1.2
18	imidazole		25.2	-7.5
19	oxazole		18.1	-3.8

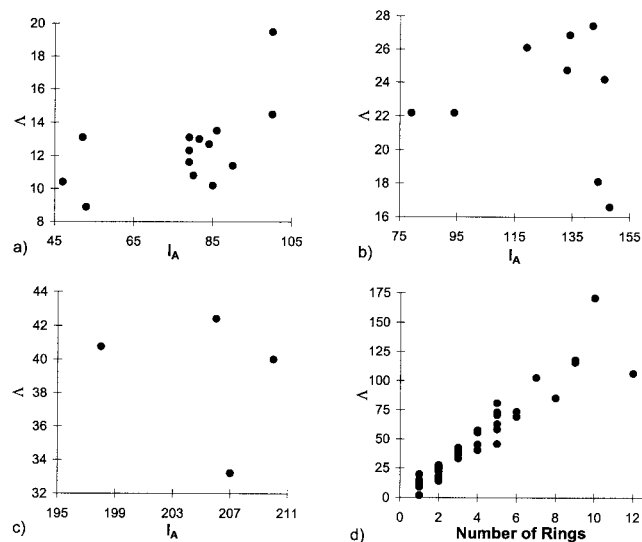
matic compounds. It is quite clear that no linear relationship exists:  $R^2$  calculated for a linear regression is 0.034.

Schleyer's results pointed out<sup>15</sup> that  $\Delta$  values are heavily dependent on the ring size and proposed a new aromaticity scale called nucleus-independent chemical shifts (NICS). Unlike  $\Delta$ , NICS values are only moderately dependent on the ring size. However NICS values presented in ref 15 show clearly that their values do depend significantly on the basis set used in the calculation. Furthermore, the NICS concept does not work well for three-membered rings due the local shielding of  $\sigma$  bonds. Further problems with the NICS definition are that it is a property which cannot be measured and that it adds local information of bonding in the ring into the total effect of a ring current of  $\pi$ -electrons. Therefore, this scale is hardly compatible with other operational definitions of aromaticity.

(15) Schleyer, P. von R.; Maerker, C.; Dransfeld, A.; Jiao, H.; van Eikema Hommes, N. J. R. *J. Am. Chem. Soc.* **1996**, *118*, 6317.



**Figure 2.** (a) Figure 1,  $\Delta$  vs RE for monocycles; (b)  $\Delta$  vs RE for cycles with two rings; (c)  $\Delta$  vs RE for cycles with three rings; (d) RE vs number of rings for all compounds.



**Figure 3.** (a)  $\Delta$  vs  $I_A$  for monocycles; (b)  $\Delta$  vs  $I_A$  for bicycles; (c)  $\Delta$  vs  $I_A$  for tricycles; (d)  $\Delta$  vs number of rings for all compounds.

We have reexamined the treatment reported by Bird.<sup>8</sup> Whereas at first sight there appears to be a moderate correlation between resonance energy (RE) and magnetic susceptibility exaltation ( $\Delta$ ) of the whole set of 59 compounds (we obtained a linear correlation with correlation coefficient of  $R^2 = 0.888$ , which is in good agreement with Bird's result), this completely disappears when monocycles<sup>16</sup> (Figure 2a) and compounds with two (Figure 2b) and three (Figure 2c) fused cycles are each considered separately: the respective correlation coefficients  $R^2$  are 0.427, 0.019, and 0.001. Indeed, we found that by using the data presented by Bird, a significantly better correlation ( $R^2 = 0.943$ ) is given by plotting the RE against the number of rings (Figure 2d) than that which he (and we) obtained plotting RE with  $\Delta$ . Analogously, Figures 3a–c shows the absence of any linear

(16) We excluded fulvene from these calculations as fulvene is not generally considered an aromatic compound, as is also consistent with its very low ASE and  $\Delta$  values: 1.9 and 1.9, respectively.

correlation of  $\Lambda$  with the aromaticity index  $I_A$  when the mono-, bi-, and tricycles are considered separately: the  $R^2$  values for Figure 3a–c are 0.339, 0.005, and 0.06, respectively. Figure 3d shows the plot of the  $\Lambda$  against the number of rings ( $R^2 = 0.902$ ). Extensive properties frequently show a good linear relationship when plotted against each other.<sup>17</sup>

While much remains to be done to define the dimensionality of aromaticity, and while the views of the

authors of the present paper are by no means in complete agreement, we believe that we have demonstrated conclusively that aromaticity is a multidimensional characteristic.

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(17) Exner, O. *J. Phys. Org. Chem.* **1997**, 10, 797.

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