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The π-Electron Delocalization Imposed by Thermal Vibrations of Substituted Benzene Analogues in Mediums of Varying Polarities

Piotr Cysewski[1,2], **Tomasz Jeliński**[1]

[1]*Department of Physical Chemistry, Collegium Medicum, Nicolaus Copernicus University*
ul. Kurpińskiego 5, 85-950 Bydgoszcz, Poland
e-mail: piotr.cysewski@cm.umk.pl
[2]*Department of General Chemistry, University of Technology and Life Sciences in Bydgoszcz*
ul. Seminaryjna 3, 85-326 Bydgoszcz, Poland

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Abstract: The unique set of aromaticity indices was identified for thermally induced changes of π-electron delocalization by means of PCA (Principal Component Analysis). It was demonstrated that solvents polarity can influence not only the values of aromaticity indices but also their contribution to Principal Components. Therefore, in different phases one should select different indices for a proper description of the aromaticity. The found aromaticity diversities indices were provided for aniline as well as *p*-nitrosoaniline and it was found that the geometry of the latter one is highly sensitive to solvents polarity changes. Thus, all of the aromaticity indices experienced a reduction of their values, with the HOMA (Harmonic Oscillator Model of Aromaticity) index being the most sensitive. It was also found that there were such vibrations which could alter this trend and lead to apparent increase of aromaticity.

Key words: aromaticity, thermal vibrations, benzene analogues, normal coordinate analysis, principal component analysis

I. INTRODUCTION

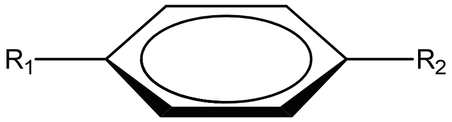
The π-electron delocalization is an unique phenomenon commonly characterizing physico-chemical properties of many organic, metalo-organic and even inorganic compounds [1-3]. Despite the fact that it does not correspond to any quantum observable many quantitative measures were proposed to interpret its occurrence [4-9]. It is commonly accepted that π-electron delocalization has a multi-dimensional nature [10]. This creates a serious problem in the formulation of any universal scale of aromaticity based on a single parameter. Two main approaches occur in literature to overcome this difficulty. One is multivariance statistical analysis based on Principal Components methods [11-14], and the second one consists in seeking non-linear relationships via neural networks in self-organizing maps [15, 16]. Both approaches intend to identify most objective and universal measures of aromaticity by utilizing commonly accepted molecular descriptors. The identification of an univocal set of indices is even more difficult due to their non-linear scaling and suffering from generalities, which was demonstrated by spectacular failures in certain situations. Different aromaticity measures do not always give consistent results among themselves [17-19] as it was reported for deviations between magnetic criteria and those based on energetic grounds [2]. Also limitations of the NICS (Nucleus-Independent Chemical Shifts) were demonstrated [21] for cases of strong anisotropy. According to recommendation proposed by Feixas et al. [17], indices including reference values should not be used for the analysis of aromaticity changes in chemical reactions. Despite all these shortcomings of aromaticity measures the universality of the phenomenon still attracts many researchers.

The calculation of aromaticity indices usually occurs for optimized molecular geometry corresponding to a global minimum on the potential energy surface. Nevertheless, it is commonly known that the geometry of all molecules at a specific temperature is not fixed and those molecules experience thermal motions. Actual deformations match normal vibrations and their amplitudes rely on frequencies of the vibrations. Hence, at some finite temperature the geometry of each molecule is not fixed and varies within some ranges of geometrical parameters. At room temperature these thermal vibrations are quite remarkable. They refer to the fact that a real molecule does not occupy a single point at the potential energy hyper-surface but is situated in a conformational region around the minimum. The frequencies of different vibrational modes determine their contributions to thermal vibrations of molecules. In our previous reports [22, 23] this aspect was brought to attention by quantification of ring skeleton flexibilities undergoing deformation along normal coordinate paths corresponding to vibrations occurring spontaneously at room temperature. As it was shown [23], the geometry alterations met during thermal vibrations are related to changes in electron delocalization and chemical shift. Also the resonance energy of the ring is affected by electron density changes along normal vibrations modes. When describing the consequences of molecular vibrations on π-electron delocalization in a benzene ring, one must consider various molecular properties. The results of PCA indicate that a proper description of the population variance of vibrating benzene structures requires four orthogonal principal components. The idea of quantification of π-electron delocalization for non-equilibrium structures comes from very well established understanding that a significant energy penalty does not take place when an aromatic ring exhibits evidential elasticity. The works of Shishkin et al. [24-26] showed that high flexibility of aromatic rings is represented by the lowest-lying molecular vibrations. A good characterization of the increase of energy between the planar equilibrium conformation and a non-planar distorted structure is the rising of the endocyclic torsion angles up to ± 20 degrees with increase of only 1.2-1.8 kcal/mol depending on the system [27, 28]. Even benzene itself in crystalline state at 20 K is non-planar [29]. Furthermore, the benzene ring can undergo large out-of-plane distortions [30-33] but its aromaticity and ring-current diamagnetism seem to be quite insensitive to such deformations of the molecule [30-34]. Such aromatic ring elasticity was documented as the common phenomenon not only for benzene analogues but it is also characteristic for heterocyclic compounds [27, 28, 35]. This is of particular importance since it provides additional degrees of freedom to biomolecules interacting in native environments.

Considering all these above stated facts, the aim of this paper is the characterization of aromaticity changes that are imposed by thermal vibrations at room temperature for seven different substituted benzene analogues undergoing thermal motions in five environments of different polarities. Also, for the assessment of the contributions of particular measures of aromaticity to the total population variance, the PCA was applied.

II. METHODS

The details of the procedure were described elsewhere [22, 23] and here only brief comments are provided. The subject of this study is presented in Fig. 1. It encompasses benzene and its seven mono- or para- substituted analogues. Five different environmental conditions were considered, namely apart from the gas phase also an implicit model of the following solvents was applied: water (ε = 78.5), acetonitrile (ε = 35.7), acetone (ε = 24.9) and THF (ε = 7.43). The values of dielectric constants are provided in parentheses. The ground state geometries of these eight highly aromatic compounds were determined by B3LYP/6-311+G** by performing full gradient optimization with a very tight option as a criterion of optimization along with an ultrafine option for grid density. The thermodynamics computations were performed for ensuring that no imaginary frequencies were assigned and the obtained structures characterized ground states. Frequencies of normal vibrations were calculated at the same level of theory within harmonic approximation. Paths along normal coordinates were identified for each of the analyzed compounds based on Hessian estimated at the same level of theory. The linear correlation between the inverse square of amplitude and thermal excitation energy documented previously [23] was applied for determination of the extreme point on the normal coordinate paths. Due to unharmoniticities typical by the first lowest laying modes they were excluded from the analysis, which does not introduce any serious limitations since these modes usually do not affect ring skeleton geometry. Both optimization and vibrational analysis were performed using the Gaussian03 program [36]. Solvents were modelled by the PCM approach implemented in the same program [37]. The explicit hydrogen with Bondi parameterization for all atoms was applied. For the set of 41 conformations (apart from the ground state also 20 others along either positive and negative directions along a normal coordinate) for each of the analyzed compounds commonly accepted aromaticity measures were estimated. They were grouped into three



	B	**Ph**	**A**	**A1**	**A2**	**A3**	**A4**
R_1	H	OH	NH_2	NH_2	NH_2	NH_2	NH_2
R_2	H	H	H	NO	NO2	CN	CHO

Fig. 1. Schematic representation of analyzed compounds

easily recognized classes. The first group comprised geometric based indices resulting from the assumption that a cooperative effect of π- and σ-orbitals leads to the unification of bond lengths within the aromatic skeleton for cyclic aromatic systems. A total of 12 aromaticity indices were utilized in this group. A normalized function of the bond lengths variance is represented by Julg and Francois (A_j) [38, 39]. LB denotes the longest bond length in the ring [40, 41], while BAC is the bond alternation coefficient developed by Krygowski and co-workers [42] and defined as root mean square deviation between successive bond lengths in the ring. Another aromaticity descriptor is the degree of uniformity of the peripheral bond orders. From two indices based on this assumption in the Pozharskii (Poz) [43, 44] index an average of absolute values of bond order is used, while the Bird's index (I_6) [45, 46] is a root-mean-square deviation of individual bond orders. A concept of an optimal bond length is used in the harmonic oscillator model of the aromaticity index (HOMA) developed by Krygowski et al. [5, 47]. This index can be divided into two independent components: energetic (EN) and geometric (GEO) contributions to the aromaticity loss with respect of the reference system. Some indices were defined on the basis of structure-to-energy relationships. An empirical formula for assessment of the ring energy content (REC) was introduced by Krygowski [41]. The HOSE parameter denotes the harmonic oscillator stabilization energy and is equal to a negative value of the energy necessary to deform the geometry of the real molecule into the geometry of one of its Kekulé structures with localized single and double bonds. Depending on the reference of single and double bonds as conjugated or isolated ones [48], two different components can be used, namely Dewar type resonance energy (DRE) and total resonance energy (TRE). The benzene ring deformation energy cost is described by the rise of energy (ΔE) imposed by excitation because direct estimation of energy-based indices was impossible.

The second set of aromaticity indices comprised 6 measures based on magnetic properties of molecules. The exaltation of magnetic susceptibility proposed by Dauben et al. [49] is defined as the difference between computed values of diamagnetic susceptibility (χ) and ones corresponding to a reference system. In the case of structures analyzed in this paper the reference system was simply the ground state of molecules. The anisotropy of magnetic susceptibility (Λ) is an index suggested by Flygare et al. [50, 51] and it is defined as a difference between out-of--plane and the average in-plane components of the tensor of magnetic susceptibility [51, 52]. The typical level of computations of these two indices is HF/6-311+G** one with the use of the CSGT method [53]. The negative value of a chemical shift of any cyclic π-electron system computed at a ring center or at some other interesting point of the system was proposed as a measure of aromaticity by Schleyer and co-workers [54, 55]. The nucleus independent chemical shift (NICS in ppm) is the most frequently estimated in the center, NICS(0), or 1 Å above it, NICS(1). Although for in-plane distortions the definition of NICS(1) is straightforward, in the case of out-of-plane deformations it not so unambiguous. This might pose a problem since obviously, on the normal coordinate paths, there is no univocal separation of in-plane and out-of-plane distortions. Thus, for preserving consistency estimation of points placements for NICS(1) computations was the same for all deformed structures. Namely, in the 3D Cartesian coordinate space the coefficients defining an equation of a plane were estimated by minimizing the distance of all ring atoms to this plane with an additional restriction of including the ring mass center. Than the line perpendicular to the plane was found, on which distance of 1 Å from the ring mass centre defined points for NICS(1) was estimated. Also a perpendicular component of the tensor is frequently used (denoted by subscript zz: NICS(1)zz or NICS(0)zz). For the computation of all four NICS-based indices the GIAO procedure at the HF/6-31G* level [56] was applied.

The third set of indices comprised electronic based measures. Changes in the number of electrons result in a response of the properties of a chemical system and this can also be a measure of aromaticity [57]. Parameters like hardness (η), electronegativity (κ) and electrophilicity (ω) were formulated using the DFT concept [58]. It is worth mentioning that in the case of compound B and A1 the molecular orbital charactering ring delocalization comes from HOMO-1 rather from HOMO as it is for other compounds analyzed here. The high electro-acceptance of the nitrosyl group imposed such alteration of the molecular orbitals sequence. No solvent related changes of the HOMO and HOMO-1 order were noticed. Electron-sharing or electronic delocalization may also be used as aromaticity measures [59]. One of such indices is the para delocalization index (PDI) proposed by Poater et al. [60]. The QTAIM theory [61-63] was used to calculate the average of the two-center electron delocalization indices (DI) [59, 64, 65] with the use of the AIMAll program [69]. The averaging of DI over two centers of all adjacent pairs of atoms around the n-membered ring results in the ATI index [61]. The index proposed by Matta and Hernandez-Trujillo [62] resembles the HOMA index; however, it uses the DI as a measure of electron-sharing alternation within a ring. The aromatic fluctuation index (FLU) [63] measures the number of electrons shared between consecutive atoms in the ring. This index is frequently expressed as a square root and denoted as FLU1/2 because of its small values. The ring critical point (RCP) characterizes, according to the QTAIM theory, the aromaticity of rings possessing delocalized π-electrons [64-66]. The electron density at RCP (ρ) and Laplacian ($\nabla 2\rho$) is particularly valuable for describing the aromaticity of different systems [67]. Also the Lagrangian (G) form of kinetic energy density and virial field (V) at RCP were used as probes of π-electron delocalization. Finally, the Shannon-like entropy introduced by Noorizadeh and Shakerzadeh [68] was used as a measure of aromaticity. The AIMAll program [69] aided in the computations related to QTAIM.

III. RESULTS AND DISCUSSION

Principal Component Analysis

The analysis of aromaticity changes induced by thermal vibrations was preceded by an assessment of mutual correlations between estimated parameters as well as the statistical significance of their contributions. In order to perform such an appraisal the PCA was applied with the use of the Statistica software package [70]. A total of 31 parameters (those described in the methodology part) were computed for structures of benzene analogues distorted along normal coordinates at room temperature. Analyzing the whole set at once could encounter severe difficulties because of highly linear dependences between distributions of some parameters and consequently singularity of resulting correlation matrix. Therefore, all aromaticity indices used in this study were divided into three groups and the PCA was performed separately for these sets. After selecting those aromaticity indices with highest contributions among each group, the final PCA was applied to a reduced set of independent aromaticity measures. The results of these two stages are presented in Fig. 2 and 3. Besides, corresponding values were collected in Table I (as well as in Tables S1-S3 in Supplementary materials). As it is demonstrated in Fig. 2, the PCA reduced the set of 12 initial geometric indices into 3 orthogonal variables covering about 90% of the population variance. Interestingly, the majority of geometric indices are highly correlated with each other (see Table S1). The first principal component covers more than 62% of the population variance and the HOMA index has the highest contribution among all geometric indices. However, as it could be expected, several other indices like GEO, A_j, Poz, BAC, LB or I_6 also have large contributions. Due to high correlations to each other and to HOMA, all these indices are statistically almost identical. The biggest contribution to the second principal component comes from the TRE index and PC2 covers an additional 18% of the population variance. Finally, the third principal component is dominated by the excitation energy of the vibrating molecules (ΔE). These conclusions confirm the findings of our previous study [23] that thermal vibrations affect aromaticity via both bond length alterations and resonance energy of the ring. The second set of analyzed indices consists of 6 magnetic measures. The details of applied PCA are presented in Table S2 and Fig. 2. It can be clearly seen that all NICS-based indices are strongly correlated to each other. Interestingly, magnetic susceptibility exaltation and its anisotropy are not particularly mutually dependent. Furthermore, there is only a very small correlation between those two parameters and all of NICS indices. The NICS values estimated at the ring centre and 1 Å above as well as their perpendicular components all have large contribution to the first principal component. Thus, for further analysis just one NICS index needs to be taken into account, namely NICS(1) having the highest contribution. This index gives a coverage of 60% of the population variance. Interestingly, also magnetic susceptibility exaltation and anisotropy has quite similar contribution the PC2. These three magnetic indices are selected for the further study. The third group of indices was the largest one and consisted of 13 electronic based indices. Application of PCA revealed that just two orthogonal variables are sufficient for the description of 87% of the total variance. Several indices have high contribution to PC1 and among them the $FLU^{1/2}$ has the largest loading. After examining the correlations between other indices, as seen in Table S3, it was found that there is only one other independent index with a significant contribution to the first principal component, namely the Laplacian of electron density ($\nabla^2\rho$(RCP)) characterizing the ring critical point. The electrophilicity and electronegativity (κ) have the largest contribution to PC2, with slightly higher loadings of the former. Since both are mutually dependent only η will be used for final analysis.

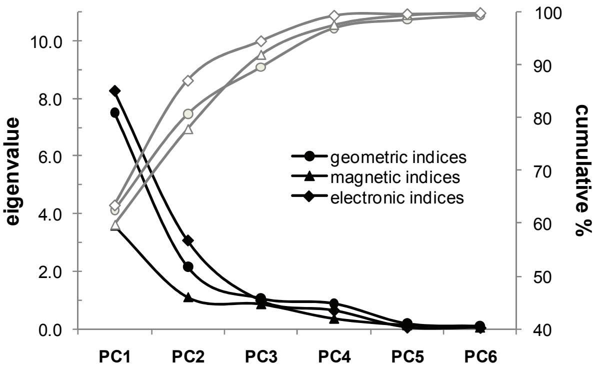


Fig. 2. The results of PCA analysis performed for different sets of aromaticity indices. The solid lines denote eigenvalues and gray style is used for cumulative percentage of total variance. The presented values correspond to structures of all analyzed vibrations ($\Delta E < 1.5$ kcal/mol) of all six compounds in five environments considered here

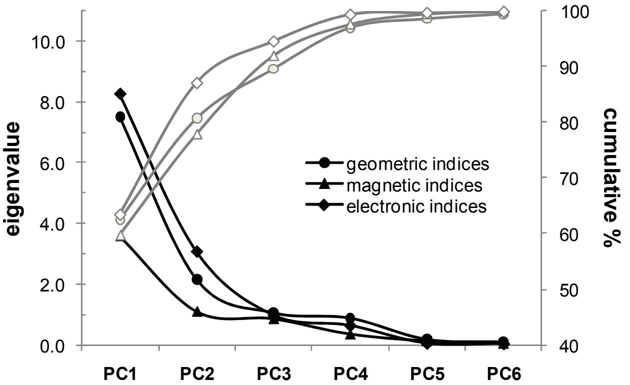


Fig. 3. The correlations between principal component loadings and dielectric constants of solvents

The procedure described above enabled the selection of indices with highest contributions to the population variance among different groups of indices. The initial number of 31 indices was reduced to 9 and all of them were used for assessment of the most significant contributions to the total variance of aromaticity changes imposed by thermal vibrations. The results of the final PCA are presented in Fig. 2 and Table 1. Four principal components with eigenvalues higher than unity were identified with a cumulative percentage of about 83% of the total variance. The highest contribution to PC1 comes from $FLU^{1/2}$. Also NICS(1) and HOMA have high loadings to PC1 but they are correlated with $FLU^{1/2}$. The PC2 is mostly determined by TRE. The highest contribution to the third principal component comes from ΔE and magnetic susceptibility exaltation dominates in PC4. Thus, after final PCA four indices were identified as preserving the majority of population variance.

Influence of the environment polarity on PC loadings

The applied PCA led to the selection of only four independent indices having the most significant contributions to new principal components. Since in our study five different environments were used, it is interesting to see if there are any correlations between the contributions of those indices to the principal components and the nature of solvents. The key parameter of a solvent that affects aromaticity is its permittivity described by the dielectric constant. In Fig. 3 changes of principal component loadings of the four selected indices as well as three other indices with high contributions to PC1 have been presented as the function of the dielectric constant of the solvents. The loadings of the first two principal components remain practically unchanged for all solvents as polar as acetone. This includes these indices of highest loadings as well as those of smaller contributions to PC1 and PC2. On the contrary, in non-polar solvents or apolar gas phase loadings of the first two principal components are smaller. This suggests that $FLU^{1/2}$ and also other correlated indices as for example HOMA are always of high significance, which is even promoted by the polar environment. Interestingly, such trend of loadings is accomplished with increase of correlation between $FLU^{1/2}$ and other geometric indices that have significant contribution to PC1. For example, the correlation coefficient between HOMA and $FLU^{1/2}$ increases from 0.47 in the gas phase up to 0.80 in the water solution. It obviously does not mean that parameters contributing to PC's are unchanged. On the contrary, since they are prone to changes by polar mediums their loadings are very high underlining their statistical significance. Slightly different behavior occurs for PC3 and PC4, for which loadings are affected only by higher polarities and remain almost the same provided that polarity is small. One can anticipate that parameters exhibiting such behavior will undergo modification by even low polarity and they stay unchanged despite the increase of polarity. This interesting conclusion drawn from the statistical analysis can be easily verified by presenting the distribution of actual indices for particular compounds in particular conditions. Finally, it is worth mentioning that, due to the observed two distinct natures of principal components, one can expect that modification of solvent polarity affects the statistical significance of aromaticity indices. Such behavior indicates not only that solvents can influence the contribution of indices to principal components but also that in different phases

Table 1. The correlation matrix between selected representative indices of aromaticity and their contributions to the dominant principal component

		1	2	3	4	5	6	7	8	PC1	PC2	PC3	PC4
1	HOMA	1.00								-0.875	-0.119	0.206	0.247
2	TRE	0.46	1.00							-0.443	**-0.753**	0.226	-0.054
3	ΔE	0.07	0.06	1.00						-0.366	0.073	**-0.656**	-0.548
4	Λ	0.18	0.10	0.09	1.00					-0.290	0.135	0.511	**-0.738**
5	χ	-0.05	0.21	0.07	-0.16	1.00				0.049	-0.642	-0.487	-0.026
6	NICS(1)	-0.78	-0.12	-0.33	-0.17	0.15	1.00			0.912	-0.270	0.093	-0.136
7	FLU$^{1/2}$	-0.76	-0.16	-0.35	-0.19	0.14	0.96	1.00		**0.923**	-0.251	0.107	-0.106
8	$\nabla^2\rho$(BCP)	0.71	0.73	0.25	0.19	0.22	-0.57	-0.59	1.00	-0.792	-0.528	0.054	-0.042
9	κ	-0.37	0.03	-0.19	-0.18	0.14	0.57	0.60	-0.17	0.582	-0.482	0.123	-0.056

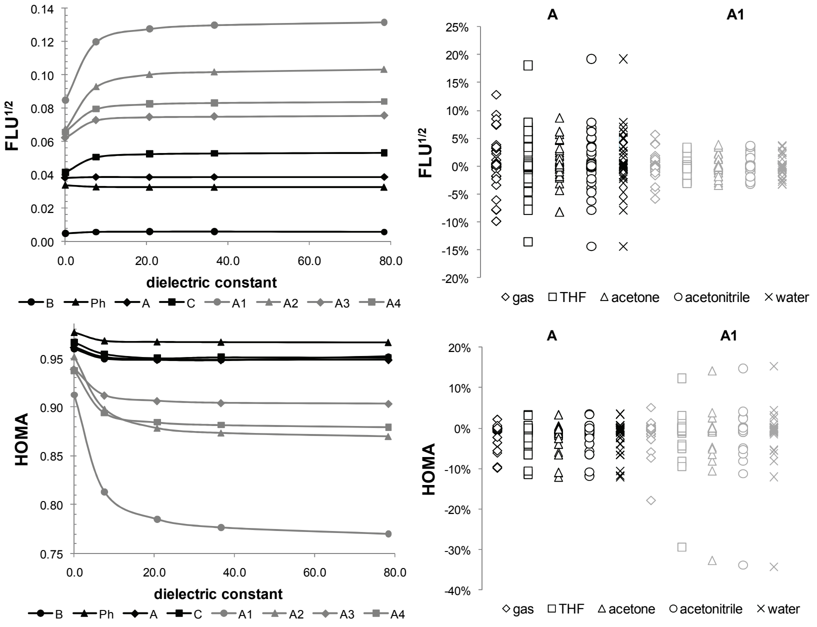


Fig. 4. The solvent influence on the FLU$^{1/2}$ and HOMA estimated for conformations corresponding to thermally excited vibrations at room temperature. On the left side the mean values of aromaticity measure were presented as a function of environment polarity, while on the right panel there are distributions of the actual values for two selected compounds (aniline (A) and *p*-nitroso aniline(A1))

one should select different indices for a proper description of the principal components.

Quantification of environment polarity on π-electron delocalization

The statistical analysis described above shows the importance of certain aromaticity indices but does not give any quantitative information about the changes of those indices induced by thermal motions. In order to describe the influence of different solvents on aromaticity measures the mean value of aromaticity indices for a specific benzene analogue undergoing thermal motions was presented as the function of the solvents polarity represented by the dielectric constant. Besides, the actual distributions of aromaticity indices were supplied for aniline and *p*-nitroso aniline. All these data were collected in Fig. 4 (and additionally Fig. 5-7 in supplementary materials). The comparison of these two compounds is interesting since the latter extends the structure of the former by an electro-donating side group, which results in very high sensitivity to polarity of the environment of such push-pull system. The altrerations of A1 geometry are more significant with the increasing polarity of the medium [70]. Consequently, its aromaticity expressed by HOMA values of the ground state geometry is seriously reduced from 0.922 in the gas phase down to 0.781 in the water solution. This is also accomplished with corresponding changes of other aromaticity descriptors although these reductions are much less pronounced. For example, the mentioned change of HOMA reached a 15% reduction with respect to the gas phase, while a similar diminution of $\nabla^2\rho$(RCP), A_j and θ is equal to only 2%, 5% and 9%, respectively. It is an interesting question whether there are any vibrations that counteract such trend of aromaticity reduction especially in polar environments. Figure 4 presents mean values of HOMA and $\text{FLU}^{1/2}$ as a function of solvent polarities. Additionally, the distribution of values of these indices are provided for two selected compounds. All para-substituted benzene derivatives are quite sensitive to solvent polarity, which leads to the more significant reduction of the mean values, the higher the dielectric constant. Besides, fluctuation of HOMA and $\text{FLU}^{1/2}$ values related to thermal motions at room temperature can reach several percent. This is interesting, since having a spectrum of structures resulting from deformation of the ground state geometry one can speculate their potential role in the cumulative effect observed as the macroscopic property. Here the π-electron delocalization is expressed by aromaticity indices that were identified by PCA as the most significant. In this sense all vibrations that lead to the reduction of aromaticity are not interesting since their potential activity is covered by the ground state or by all those geometries that are responsible for the increase of aromaticity measures. The most interesting are such vibrations which lead to apparent increase of aromaticity indices. Indeed, one can find such modes. For example, for A1 the vibration corresponding to 858 cm^{-1} has a character of in-plane symmetric ring breathing taking place mainly in the direction perpendicular to the line defined by both side groups. The HOMA values estimated along the path defined by this normal mode can alter from 0.513 after ring shrinking (negative direction) up to 0.899 after expansion (positive direction). This stands for 15% increase of this measure of aromaticity in the latter case. Interestingly, also other indices are affected by this vibration. For example, 14% increase of TRE has been noticed. Also $\nabla^2\rho$(RCP) values rise by 7% is associated with 2% reduction of $\text{FLU}^{1/2}$ values. This effect is rather small but interesting and consistent with most significant measures of aromaticity.

IV. CONCLUSIONS

A proper set of aromaticity indices was selected for thermally induced changes of π-electron delocalization by using PCA. It is clear that for a proper description of the population variance of distorted benzene analogue structures indices from three different index classes are necessary. The applied PCA analysis revealed that four orthogonal components are sufficient for describing 83% of the population variance. The principal component loadings of selected indices varied depending on the polarity of a solvent and two groups of indices are to be distinguished. The loadings of the first two principal components are relatively small in non-polar solvents and in the gas phase, while in solvents as polar as acetone they are larger and remain almost unchanged despite the increase in polarity. In the case of PC3 and PC4 their loadings are affected by solvents of high polarity which reduce them, but when the polarity is low they remain rather stable. This interesting observation leads to the conclusion that polarity of solvents affects statistical significance of aromaticity indices. Therefore, because of the changes in contributions of indices to principal components, their proper description requires a selection of different indices depending on the phase used.

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SUPPLEMENTARY MATERIALS

The values presented in Tables S1-S3 correspond to structures of all analyzed vibrations (ΔE <1.5 kcal/mol) of all seven compounds (B, Ph, A, A1, A2, A3, A4) in five distinct environments (gas phase, ε = 7.43 for THF, ε = 24.9 for acetone, ε= 35.7, acetonitrile and ε = 78.5 for water).

Table S1. The correlation matrix between geometry-based indices and their contributions to the most significant principal components. Dominant contributions are marked in bold face style

		1	2	3	4	5	6	7	8	9	10	11	PC1	PC2	PC3
1	ΔE	1.00											-0.115	-0.029	**0.857**
2	HOMA	0.06	1.00										**-0.973**	0.013	0.019
3	GEO	-0.05	-0.92	1.00									0.938	0.254	0.131
4	EN	-0.05	-0.79	0.48	1.00								0.696	-0.427	-0.246
5	A_j	0.05	0.92	-1.00	-0.47	1.00							-0.936	-0.258	-0.135
6	BAC	-0.14	-0.87	0.94	0.47	-0.94	1.00						0.943	0.220	0.071
7	I_6	0.10	0.88	-0.95	-0.47	0.95	-0.98	1.00					-0.944	-0.272	-0.060
8	Poz	0.12	0.87	-0.94	-0.46	0.94	-0.99	0.96	1.00				-0.936	-0.197	-0.104
9	LB	-0.07	-0.90	0.85	0.67	-0.85	0.87	-0.91	-0.85	1.00			0.953	-0.037	-0.008
10	REC	0.17	0.71	-0.46	-0.87	0.45	-0.49	0.48	0.47	-0.73	1.00		-0.709	0.584	0.260
11	TRE	0.05	0.46	-0.26	-0.61	0.26	-0.30	0.24	0.32	-0.49	0.81	1.00	-0.487	**0.857**	-0.063
12	DRE	-0.11	-0.11	0.16	0.00	-0.16	0.12	-0.21	-0.07	0.07	0.19	0.73	0.056	0.785	-0.380

Table S2. The correlation matrix between magnetic indices and their contributions to the dominant principal component

		1	2	3	4	5	PC1	PC2
1	Λ	1.00					0.248	**0.699**
2	χ	-0.16	1.00				-0.225	**-0.742**
3	NICS(1)	-0.17	0.15	1.00			**-0.982**	0.093
4	NICS(1)$_{zz}$	-0.11	0.08	0.83	1.00		-0.852	0.179
5	NICS(0)	-0.19	0.21	0.90	0.68	1.00	-0.934	0.009
6	NICS(0)$_{zz}$	-0.17	0.14	0.95	0.74	0.89	-0.953	0.092

Table S3. The correlation matrix between electronic-based indices and their contributions to the dominant principal component

		1	2	3	4	5	6	7	8	9	10	11	12	PC1	PC2
1	η	1.00												-0.848	0.480
2	κ	-0.59	1.00											0.314	-0.738
3	ω	-0.80	0.95	1.00										0.544	**-0.718**
4	PDI	0.93	-0.38	-0.62	1.00									-0.911	0.318
5	FLU$^{1/2}$	-0.92	0.35	0.60	-0.99	1.00								**0.914**	-0.299
6	θ	0.94	-0.35	-0.60	0.99	-0.99	1.00							-0.911	0.298
7	ATI	0.92	-0.34	-0.58	0.99	-0.98	1.00	1.00						-0.913	0.275
8	ρ(RCP)	0.33	0.14	-0.03	0.46	-0.47	0.46	0.48	1.00					-0.757	-0.629
9	$\nabla^2\rho$(RCP)	0.49	0.01	-0.17	0.59	-0.59	0.60	0.61	0.97	1.00				**-0.852**	-0.497
10	V(RCP)	-0.46	-0.01	0.17	-0.55	0.56	-0.56	-0.58	-0.98	-0.99	1.00			0.835	0.513
11	G(RCP)	0.48	0.01	-0.17	0.57	-0.58	0.58	0.60	0.98	1.00	-1.00	1.00		-0.847	-0.505
12	HESS	0.49	0.01	-0.17	0.59	-0.59	0.60	0.61	0.97	1.00	-0.99	1.00	1.00	-0.852	-0.497
13	SA	-0.45	0.18	0.32	-0.60	0.65	-0.55	-0.54	-0.38	-0.41	0.40	-0.41	-0.41	0.608	-0.105

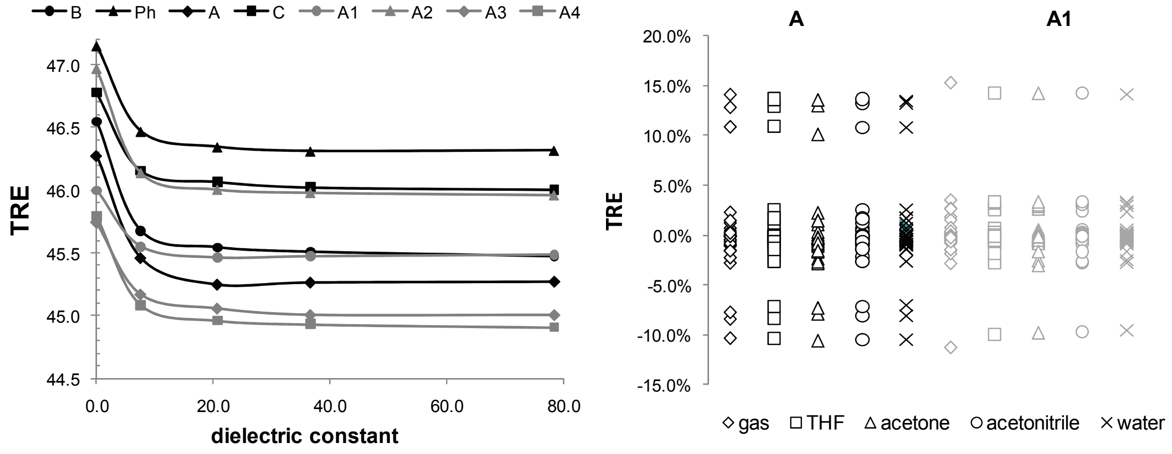

Fig. 5. The solvent influence on TRE and values estimated for structures corresponding to thermally excited vibrations at room temperature. Notation is the same as in Fig. 4

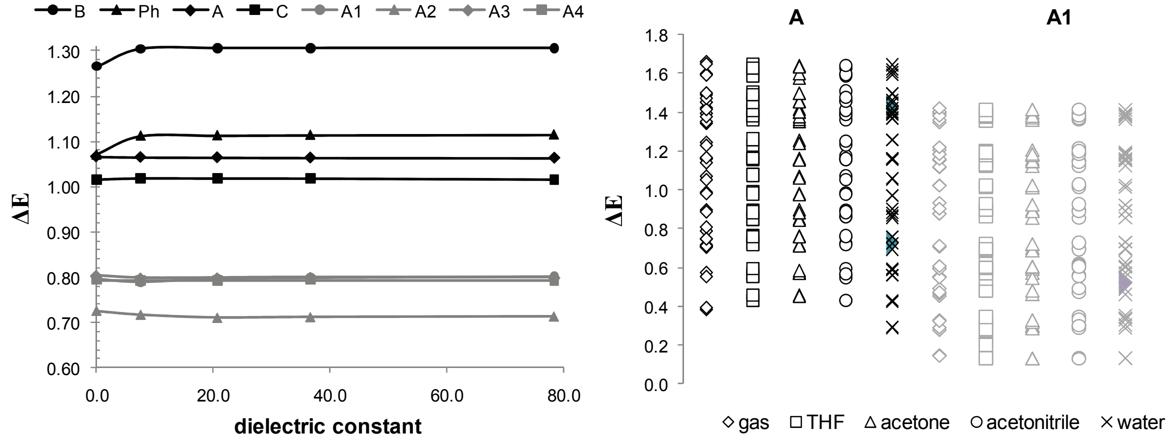

Fig. 6. The mean value of θ correlated with the solvents dielectric constant

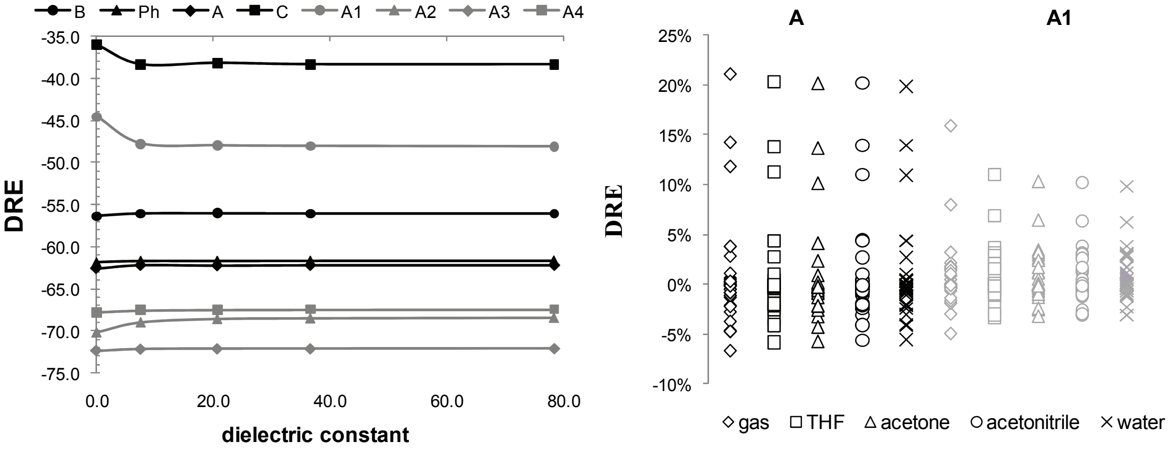

Fig. 7. The mean value of DRE correlated with the solvents dielectric constant

PIOTR CYSEWSKI, PHD, DSCI. is Director of the Physical Chemistry Department, Ludwik Rydygier Collegium Medicum of Bydgoszcz, Nicolaus Copernicus University in Toruń, ul. Kurpińskiego 5, 85-950 Bydgoszcz, Poland. Graduate of the Nicolaus Copernicus University in 1984, he presented his PhD dissertation at this University four years later. In 2000, he reached the DSci level at the Institute of Bioorganic Chemistry, Polish Academy of Sciences in Poznań. Since 2006, he has been holding the Professor position at the Nicolaus Copernicus University. Also since 2004, he has been Professor of the University of Technology and Natural Sciences in Bydgoszcz. He utilizes molecular modeling tools to describe properties of bio-organic compounds. Apart from hydroxyl radical analogues of nucleobases also mechanisms of radical polymerizations, aromatic properties of organic compounds, stacking interactions, recognition patterns, telomeric B-DNA structure and dynamics are his particular interest. Main scientific interests comprise (i) molecular basis of observed biochemical consequences of free radical modified nucleobases and nucleosides, especially tautomeric equilibriums, protolytic properties, coding abilities, inter-strand and intra-strand stacking, N-glycosidic bond stabilities, etc. (ii) structural and energetic diversities of modified double stranded DNA in different polymorphic forms (iii) environment influence on the heterogeneities of aromaticities of amino acids, canonical and modified nucleobases and (iv) intermolecular interactions with amino acids as the source of recognition of modified nucleobases. He is an author of 65 papers in peer reviewed journals.

TOMASZ JELIŃSKI, MD, was born in Bydgoszcz, Poland in 1986. He studied chemistry at the University of Technology and Life Sciences in Bydgoszcz, where he received his M.Sc. in Chemical Technology. Since 2011 he has been working toward earning his Ph.D. in the Physical Chemistry Department at the Nicolaus Copernicus University, Ludwik Rydygier Collegium Medicum of Bydgoszcz under the supervision of Prof. Cysewski.