

Sigma- and pi- electron structure of aza-azoles

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Abstract The reasons behind changes of aromaticity in 10 unsubstituted aza-azoles were analysed by employing the natural bond orbital (NBO) approach at the MP2/6-311+G(d,p) level of theory. Sum of occupations of p_z orbitals at atoms in the ring correlates well with the magnetism based aromaticity index NICS as well as with the number of nitrogen atoms in the ring. Changes of NICS depend strongly in a linear way on the number of NN bonds. Classification of azoles based on the number of pyridine-type nitrogen atoms vicinal to NH is supported by plotting the relative occupation of π orbitals (π_{occ}) against the relative occupation of σ orbitals (σ_{occ}) for all individual atoms in rings.

Keywords Aromaticity · Azoles · HOMA · NBO · NICS · pEDA · sEDA

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Introduction

Azoles belong to an interesting and important class of π -electron systems [1, 2], which fulfill the Hückel $4n+2$ rule but have different degrees of aromaticity [3]. In aza-azoles the aromatic stabilization energy (ASE) depends on the number and location of the pyridine-type nitrogen atoms in the ring, especially how many pyridine-type nitrogen atoms are next to the pyrrole-type nitrogen atom [4]. The pyrrole-type nitrogen possesses an electron lone pair perpendicular to the molecular plane and nominally contributes two electrons to the aromatic sextet. There can also be up to four pyridine-type nitrogen atoms, each of them contributes a single electron to the electronic sextet from a $2p_z$ orbital and their lone pairs lie in the ring plane. These two types of nitrogen atoms, and also the carbon atoms present in the ring, have their own σ -electron structure, which may in some way interfere with the π -electron structure, and contribute to the picture of π -electron delocalization. There is a long-standing dispute about how far π -electron delocalization or σ -electron structure is responsible for aromatic equalization of bonds length and other aromatic properties [5–10]. A number of approaches have shown either significant colinearities between some aromaticity indices or lack of correlation [11–13]. These contradictions may be due to different physical/chemical bases for the indices themselves or to specific relationships between σ - and π - electron contributions to the properties taken to measure “aromatic character”. Hence, in this paper we investigate the interrelationship between the σ - and π -electron structures in aza-azoles.

Methods

Geometry optimizations and all other calculations were performed at the MP2/6-311+G(d,p) level of theory using

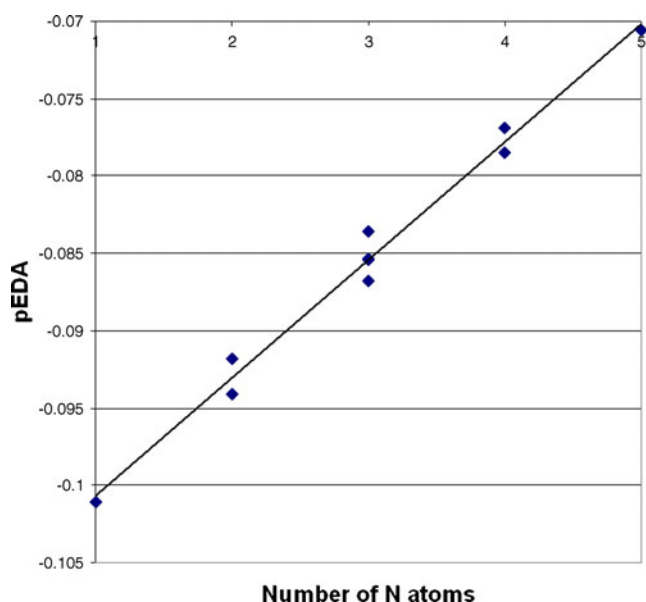


Fig. 1 The linear relationship between *pEDA* and the number of nitrogen atoms in azoles. Regression equation: $y = 0.0076x - 0.1083$; $CC = 0.993$

the Gaussian 03 suite of programs [14]. All optimizations were followed by frequency calculations to ensure that the calculated stationary points are true minima on the potential energy surface. Natural bond orbital (NBO) [15] analysis was performed by NBO 5.G program interfaced to Gaussian03 using MP2 density matrix with the keyword

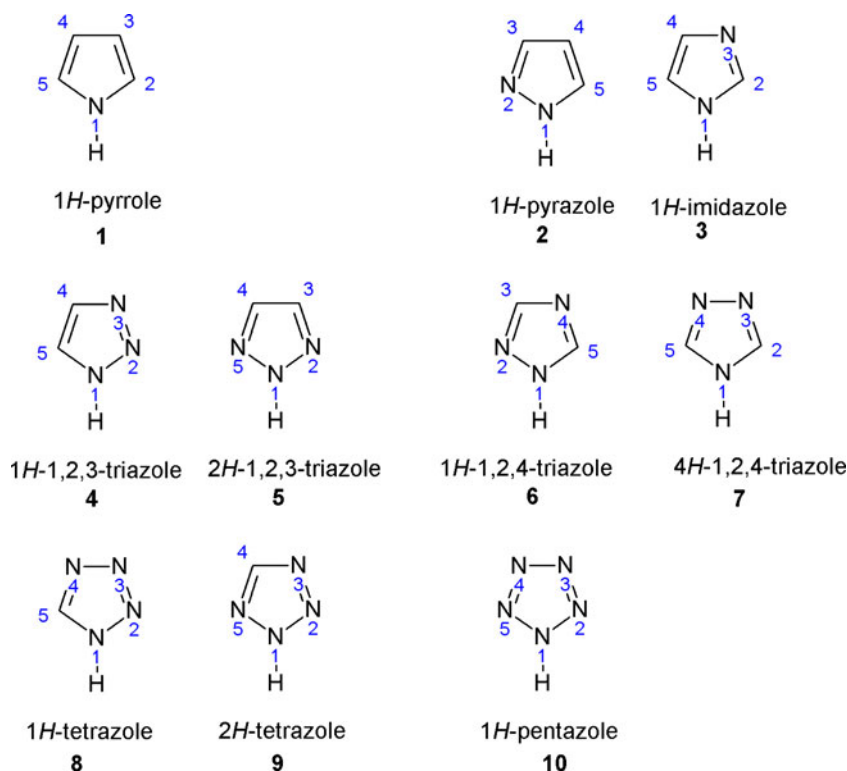
density=current. The NICS [16] aromaticity index was calculated as a shielding constant (taken with minus sign) of a ghost atom located at the geometric center of the ring and NICS(1) was calculated 1 Å above the ring.

Results and discussion

To analyze separately σ - and π -electron distributions we employed an occupation partitioning scheme based on natural population analysis (NPA). This partitioning scheme is based on NBO analysis, which is well known for producing reliable results for organic compounds, comparing to other charge partitioning methodologies like Mulliken population analysis which is strongly basis set dependent. The advantage of NPA approach lies also in the ease of separation of σ - and π -electronic systems in the case of flat aromatic molecules. If the molecule is oriented in the *xy* plane the *s*, *p_x* and *p_y* natural atomic orbitals (NAOs) occupations can be directly assigned to σ -electronic system and the *p_z* NAOs occupations to π -electronic system. We used similar approach in our previous study about substituted benzene molecules [17].

In our approach the σ -electron population of the ring is calculated as a sum of the populations of the *s*, *p_x* and *p_y* natural atomic orbitals of the ring atoms. Subtracting the “nominal” number of σ electrons expected for the studied system, expressed by variable “*C*” (see Eq. 1), gives the

Scheme 1 Pyrrole and the aza-azoles



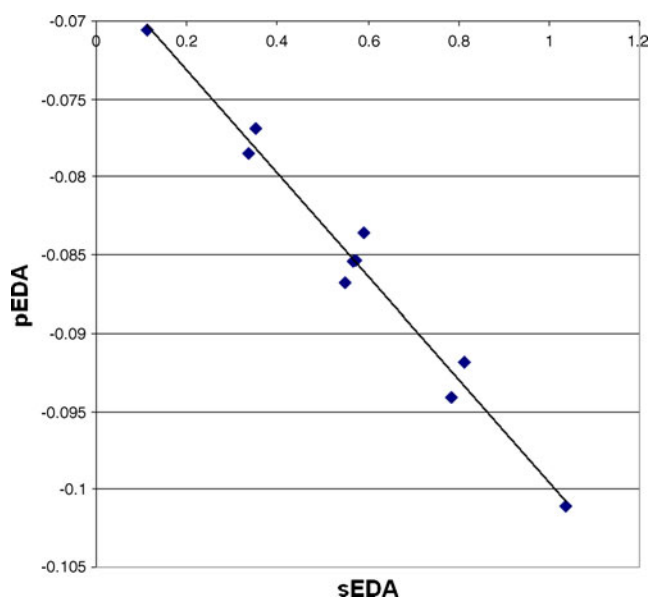


Fig. 2 The inter-relationship of total-ring $pEDA$ on $sEDA$. Regression equation: $y = -0.0329x - 0.0666$; $CC = 0.987$

extent to which the studied system deviates from the “nominal” distribution: this value we call $sEDA$ [sigma Electron Donor-Acceptor]. The parameter “C” changes in the series of azoles because a pyrrole-type nitrogen atom contributes only three electrons to the σ -system (like carbon) but each pyridine-type nitrogen atom contributes four electrons to the σ -system. Thus, the value of “C” is equal to 15 in the case of pyrrole **1** but is incremented as

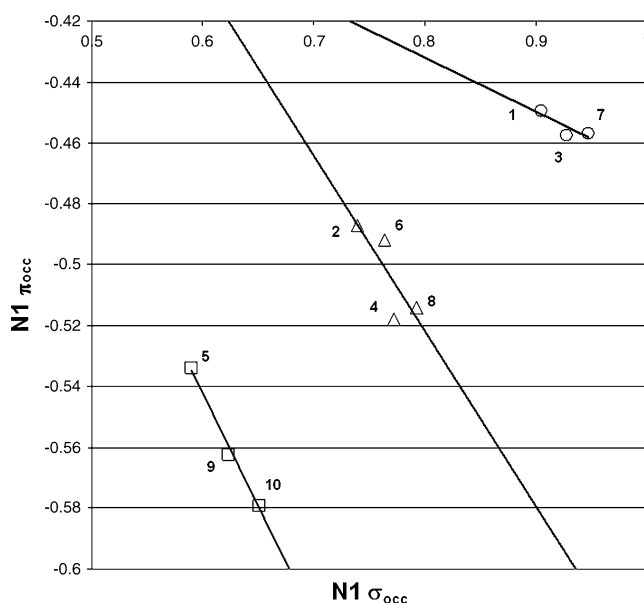


Fig. 3 The inter-relationship of pyrrole-type nitrogen π_{occ} on σ_{occ} (left: $y = -0.7399x - 0.0988$; $CC = 0.995$)(middle: $y = -0.5743x - 0.0625$; $CC = 0.811$)(right: $y = -0.1772x - 0.2904$; $CC = 0.851$)

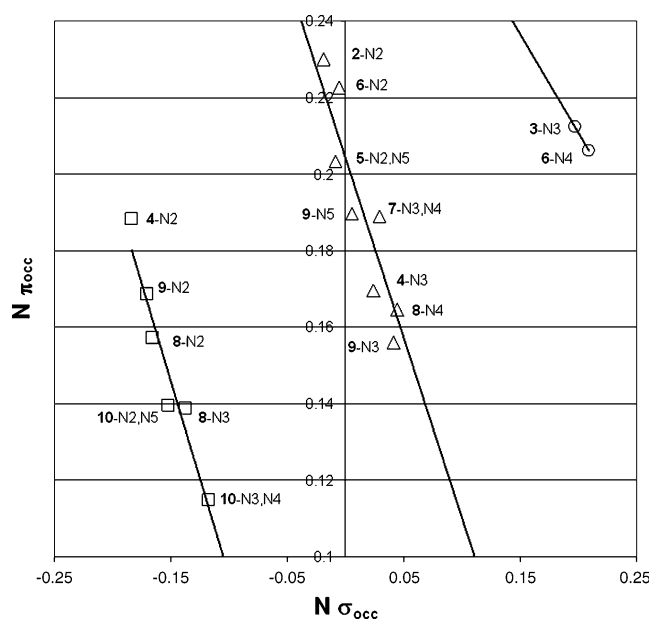


Fig. 4 The inter-relationship of pyridine-type nitrogen π_{occ} on σ_{occ} (left: $y = -1.0181x - 0.0069$; $CC = 0.969$)(middle: $y = -0.9391x + 0.204$; $CC = 0.892$)(right: $y = -0.5152x + 0.3138$; $CC = 1$)

the number of pyridine-type atoms increases, reaching the maximum value of 19 for pentazole **10**.

Similarly, the $pEDA$ [π Electron Donor-Acceptor] parameter is obtained by summing up the populations of the p_z natural atomic orbitals (perpendicular to the molecule plane) and subtracting the “nominal” value of 6 (two electrons from pyrrole-type nitrogen atoms and one electron

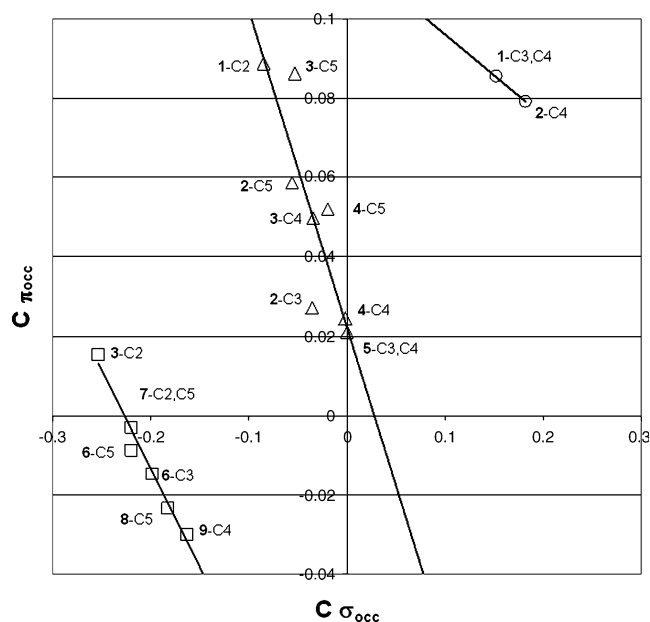
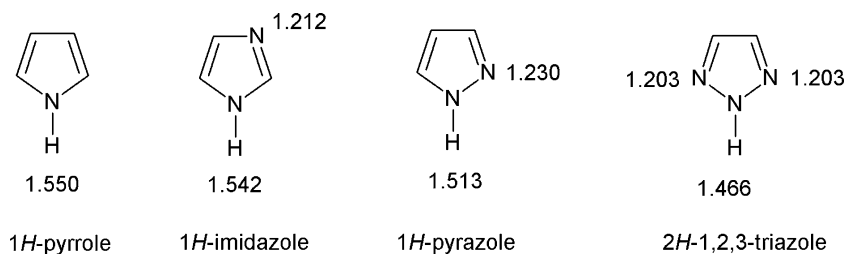


Fig. 5 The inter-relationship for carbon atoms: π_{occ} on σ_{occ} (left: $y = -0.4967x - 0.113$; $CC = 0.986$)(middle: $y = -0.7975x + 0.0223$; $CC = 0.881$)(right: $y = -0.2058x + 0.1168$; $CC = 1$)

Scheme 2 Total occupations of nitrogen p_z natural atomic orbitals of selected azoles



from each other atom). Thus, $pEDA$ [Eq. 2] expresses the deviation from the “nominal” or “ideal” value of the electronic sextet.

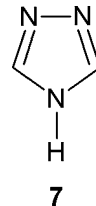
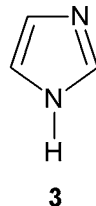
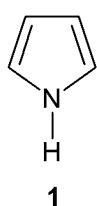
$$sEDA = \sum_{j=1}^5 \sigma^j - C \quad (1)$$

$$pEDA = \sum_{j=1}^5 \pi^j - 6 \quad (2)$$

Scheme 3 Azoles showing HOMA and ASE (italic) values together with $HOMA_{\text{mean}}$ and ASE_{mean} for each sub-group

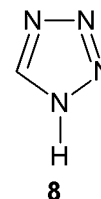
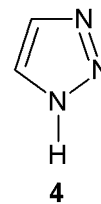
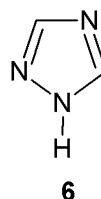
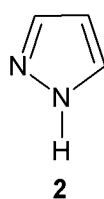
Sub-group " $N_{2,5}=0$ " $HOMA_{\text{mean}} = 0.870$, $ASE_{\text{mean}} = 18.1$

0.876 (20.57) 0.908 (18.78) 0.827 (14.96)



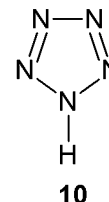
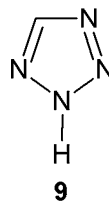
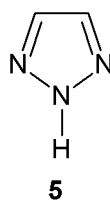
Sub-group " $N_{2,5}=1$ " $HOMA_{\text{mean}} = 0.924$, $ASE_{\text{mean}} = 21.9$

0.926 (23.70) 0.938 (21.33) 0.931 (24.37) 0.900 (18.26)



Sub-group " $N_{2,5}=2$ " $HOMA_{\text{mean}} = 0.944$, $ASE_{\text{mean}} = 26.6$

0.960 (26.66) 0.924 (26.49) 0.948



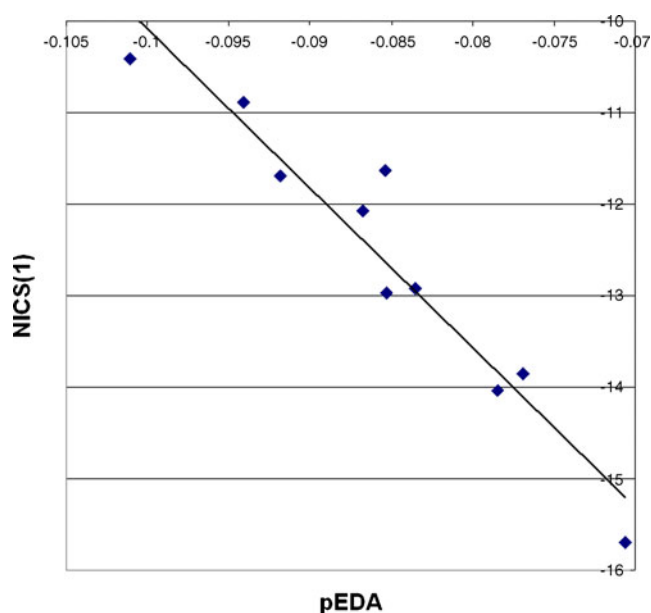


Fig. 6 The inter-relationship of NICS(1) on $pEDA$. Regression equation: $y = -173.85x - 27.466$; $CC = 0.9583$

Azoles may be classified [4] according to the number ($N_{2,5}$) of pyridine-type nitrogen atoms neighboring the NH group in the ring. Thus, the “ $N_{2,5}=0$ ” group are pyrrole **1**, 1*H*-imidazole **3** and 4*H*-1,2,4-triazole **7**, the “ $N_{2,5}=1$ ” group are 1*H*-pyrazole **2**, 1*H*-1,2,3-triazole **4**, 1*H*-1,2,4-triazole **6** and 1*H*-tetrazole **8**, and the “ $N_{2,5}=2$ ” group are 2*H*-1,2,3-triazole **5**, 2*H*-1,2,3-tetrazole **9** and pentazole **10**. When $pEDA$ values are plotted against $sEDA$ values for all ten azoles (Scheme 1), the observed correlation is expected since the π -structure may only take electrons from the σ -structure. Figure 2 presents this dependence ($CC = -0.987$).

It should be noted that changes in $pEDA$ are dramatically smaller than those for $sEDA$. When the CH units are replaced by pyridine nitrogen atoms the total π -population of the ring increases and the σ -population decreases. The decrease of σ -population is partially because hydrogen atoms are source of electron density for σ -system and the number of hydrogen atoms becomes smaller and smaller when consecutive CH groups are replaced by N atoms.

Deeper analysis of the above relationship (Fig. 2) is achieved by plotting the relative occupation of π orbitals (π_{occ}) against the relative occupation of σ orbitals (σ_{occ}) for individual atoms. In this way are obtained three scatter plots: two for the two types of nitrogen atom (Figs. 3 and 4) and one for the carbon atoms (Fig. 5).

When all the points are taken into account, lack of a good correlation in the scatter plots in Figs. 3, 4 and 5 is not unexpected. Atoms participating in the ring differ in their electronegativities (pyrrole-type, pyridine-type and carbon) and also in their close environment. Nevertheless, a general trend is common to all three relationships: the slopes are

positive indicating the necessity that if the σ structure becomes richer in electrons then the π structure must lose them. However in all three cases (Figs. 3, 4 and 5) three well-separated clusters (or subsets) can be observed for which the slopes are negative. The plots show that the changes in σ/π relationships depend on the electronegativity of atoms involved in the whole structure of azoles, as well as their neighborhood. Moreover, the clusters are grouped following the rule dependent on the number of 2,5 pyridine-type nitrogen atoms neighboring the relevant atom.

For the dependence of orbital occupations of pyrrole-type nitrogen N1 π_{occ} on N1 σ_{occ} , (Fig. 3), the type “ $N_{2,5}=2$ ” systems lose more π electrons than those of type “ $N_{2,5}=1$ ” and these still less than for type “ $N_{2,5}=0$ ”. This rule is nicely illustrated by showing the occupation on these atoms in the four simplest cases: for pyrrole **1**, imidazole **3**, pyrazole **2** and 2*H*-1,2,3-triazole **5**, as shown in Scheme 2.

The highest occupation on the pyrrole-type nitrogen occurs in pyrrole **1**, where there are no interactions with any nitrogen atoms, then for imidazole **3**, where the pyridine-type nitrogen atom is distant. For the examples of neighboring one “ $N_{2,5}=1$ ” and two “ $N_{2,5}=2$ ” pyridine-type nitrogen atoms (**3** and **5**), the occupation on the pyrrole-type nitrogen atom decreases significantly. Thus, it may be concluded that direct interactions between pyridine-type nitrogen and pyrrole-type nitrogen atoms is the most effective factor for delocalization of p_z electrons from pyrrole nitrogens towards the vicinal nitrogen atoms and then further in the ring. This observation can be rationalized as follows: electronegative nitrogen atoms replacing CH

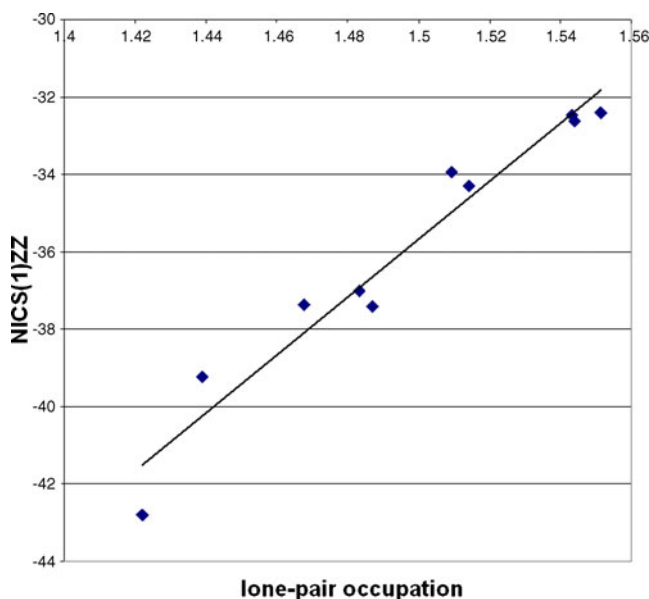


Fig. 7 Dependence of NICS(1)_{ZZ} on lone-pair orbital occupation. Regression equation: $y = 74.71x - 147.73$; $CC = -0.9745$

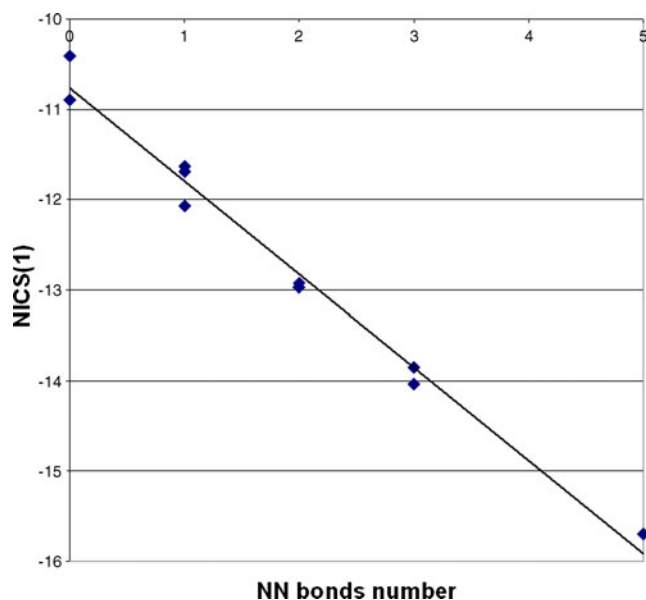
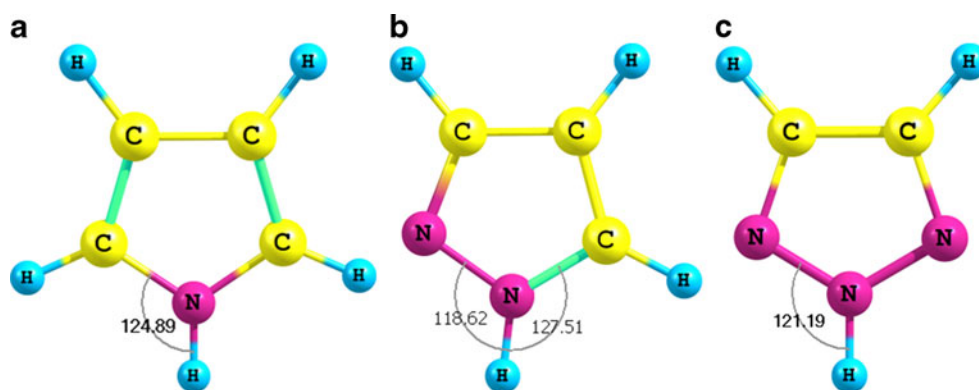


Fig. 8 The inter-relationship of NICS(1) on the number of NN bonds. Regression equation: $y = -1.0294x - 10.765$; $CC = 0.9922$

cause a decrease of π electron occupation on the p_z orbital of the pyrrole-type nitrogen atom relative to the effect due to less electronegative carbon atoms. The electron pair of this nitrogen atom is drawn out to the ring as the number of electronegative pyridine nitrogen atoms increase, replacing less electronegative carbon atoms. The σ system of the ring may withdraw electrons also from C-H bonds by means of an inductive effect. As the consecutive pyridine-type nitrogen atoms are introduced into the ring the number of C-H bonds is decreasing so the possibility to draw σ electrons into the ring is also decreased.

For the dependence of pyridine-type nitrogen $N \pi_{occ}$ on $N \sigma_{occ}$, (Fig. 4) a similar trend is observed. Again, three classes of pyridine nitrogen form clusters, according to the number of nitrogen atoms directly bonded to the relevant nitrogen atom, and the slopes are again negative. In each cluster, the more nitrogen atoms, then the lower is π_{occ} . Similarly, for the dependence of carbon atoms $C \pi_{occ}$ on $C \sigma_{occ}$, (Fig. 5), the slopes in clusters are also negative and

Fig. 9 Angles XNH (X=C or N) for molecule of class “0” (a), of class “1” (b) and of class “2” (c)



the occupation of the π -orbital on a carbon atom increases with a decrease of the number of nitrogen atoms.

We conclude that two factors, which are not always independent, play an important role in deciding the relationship between σ - and π -electron structure in azoles. The first factor is the number of pyridine-type nitrogen atoms ($N_{2,5} = 0, 1$ or 2) neighboring the pyrrole nitrogen (NH), and the second is the number of CH units replaced by pyridine-type nitrogen atoms.

One more interesting symptom of the dependence of π -electron structure on the relative locations of pyridine- and pyrrole-type nitrogen atoms is that mean HOMA values for the subgroups [4] “ $N_{2,5} = 0$ ”, “ $N_{2,5} = 1$ ” and “ $N_{2,5} = 2$ ” increase as N increases, as shown in Scheme 3. Similarly, mean ASE values (taken from [3]) distinguish between these three subgroups.

The population of electrons located on π orbitals in the ring ($pEDA$) is nicely related to the aromaticity index NICS (1) [18] indicating that $pEDA$ may also act as a quantitative measure of azole aromaticity. Since the population of π -electrons depends on their delocalization from the pyrrole-type nitrogen atom, the less π -electrons are present on this atom, the more they are delocalized on the ring and the more aromatic is the ring as measured by delocalization indices such as NICS(1). The correlations in Figs. 6 and 7 support this view. The greater value of $pEDA$, i.e., the population of π -molecular orbitals, the more negative NICS (1), i.e., the more aromatic the system in question. The same type of dependence is present for NICS(1) or NICS (1)_{zz}. When NICS(1) values are plotted against the number of NN bonds, a linear relationship is significant, as shown in Fig. 8.

The data from Scheme 3 show one more interesting feature. The averaged ASE and HOMA values for azole subgroups $N_{2,5} = 0, N_{2,5} = 1$, and $N_{2,5} = 2$ increase with an increase of the number of possible interactions between the NH group and a lone pair of a pyridine-type nitrogen atom. These interactions are associated with the change of HNN angles in molecules that are unsymmetrical and the values are smaller than those observed for HNC angles. The

averaged value for three cases with one-sided (lone pair)/NH interactions [*1H*-pyrazole **2**, *1H*-1,2,3-triazole **4** and *1H*-124-triazole **6**] is 119.1° whereas for (lone pair)/CH interactions [pyrrole **1**, imidazole **3** and *4H*-1,2,4-triazole **7**] the averaged value is 126.2°. Evidently, the attraction between lone pair and NH-bond decreases the angle. Moreover, as results from Scheme 3 indicate, the number of such interactions is also associated with an increase of aromaticity, i.e., the ASE and HOMA values. It is also interesting to note that natural charges on pyrrole-type nitrogen atoms are for $N_{2,5}=0$, $N_{2,5}=1$ and $N_{2,5}=2$ type atoms $\sim 0.53e$, $\sim 0.33e$ and $\sim 0.13e$, respectively, indicating that pyridine/pyrrole NH interactions decrease charge on the NH nitrogen atom.

An increase of ASE on a sequence of systems belonging to subgroups $N_{2,5}=0$, 1 and 2 is nicely associated with the change of structure, i.e., the value of angle XNH - α . For subclass " $N_{2,5}=0$ " $\alpha=124.9$. for subclass " $N_{2,5}=1$ ", where the interaction is one sided $\alpha=118.6$, and for symmetric class " $N_{2,5}=2$ " $\alpha=121.2$. A reasonable explanation is that interaction of lone pair with N-H dipole (Fig. 9b) is attractive, and thus may be stabilizing the system in question.

Conclusions

Occupation of molecular π orbitals in azoles depends linearly on the number of nitrogen atoms: the more nitrogen atoms then the higher occupation.

Classification of aza-azoles by counting NH/N- lone pair interactions ($N_{2,5}$) is documented by dependences of *pEDA* on *sEDA* estimated for pyridine-type nitrogen, pyrrole-type nitrogen and carbon atoms. The three classes of azoles ($N_{2,5}=0$, 1 or 2) clearly differ when aromatic stabilization energies (ASE) or HOMA values are compared.

Aromaticity of azoles follows an additivity rule: NICS(1) correlates linearly with the number of NN bonds as well as with the number of nitrogen atoms.

Interactions between NH bond and the lone pair of the neighboring pyridine-type nitrogen atom lead to a dramatic decrease of CNH angle: 118.6° for pyrazole compared to 124.9° for pyrrole.

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