J. Org. Chem. **2001,** *66,* 8737−8743

Application of Natural Bond Orbital Analysis to Delocalization and Aromaticity in C-Substituted Tetrazoles

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Received January 18, 2001

Energies of two tautomeric forms of 10 tetrazole derivatives substituted at C5 were established by DFT/B3LYP calculations carried out at the 6-311++G** level. In each case the calculated energy of the 2H-tautomer was lower than that of the 1H. Furthermore, three geometric aromaticity indices of both forms were calculated, as were the values of nuclear independent nuclear shift and aromatic stabilization energy. The electronic properties were evaluated with the help of the natural bonding orbital theory. Following this a new π-delocalization parameter, the root-mean square of π-electron density localized on the atoms of the five-membered tetrazole ring, SDn, was introduced. It was concluded that the electronic delocalization can be described equally well by three different parameters: SDn, the extent of the transfer of electron density from the p_z orbital of one nitrogen to the rest of the π electron system, and population of two antibonding π* orbitals. Arguably, the information provided by the electronic parameters is similar to that contained in the geometric (structural) aromaticity indices except for tetrazole substituted by $-BH_2$.

Introduction

The tetrazole ring is a 6π-azapyrrole-type system that can exist in two tautomeric forms.[1] Many tetrazole derivatives exhibit biological activity.[1] The dynamic development of tetrazole chemistry during the past 20 years can be attributed to their wide application in medicine, biochemistry, agriculture, photography, information recording systems, explosives, and others.[1c,2] It can be inferred from the experimental data on mass spectrometry[3] and photoelectron spectroscopy[4] that the 2H-tetrazole is more stable than the 1H-tautomer in the gas phase. However, microwave spectroscopy has indicated that both tautomeric forms of tetrazole exist in the gas phase,[5] and some investigators have claimed that in a nonpolar solvent (dioxane) 1H-tetrazole is dominant.[6,7] On the other hand, theoretical calculations have shown that, in the gas phase, the 2H continues to be the lowest energy tautomer on the semiempirical,[8] ab initio HF,[9−11] and DFT levels[12] and that tautomerism in tetrazole depends on the electric properties of the medium.[10,12] In solutions of nonpolar solvents, tetrazole should occur in the 2H-tautomeric form.

Replacement of one of the hydrogens leads to three possible types of monosubstituted tetrazoles with substituents at position 1, 2, or 5. Derivatives of tetrazole substituted at C5 can also exist in two tautomeric forms as shown in Figure 1.

It seemed interesting to us to see whether the tautomerism in tetrazole C5-derivatives is dependent on the electronic structure of the substituents. However, experimental data on tautomerism of tetrazole derivatives is scarce. One hint is that, for 5-phenyltetrazole, a comparison of polarized absorption spectra in poly(vinyl alcohol) with calculated (CNDO/S) transition moment directions has made it possible to establish the dominant species in the medium to be the 2H-tautomer.[13] Another is that for 5-methoxy-tetrazole in the gas phase the ionization potential and orbital energy correlate better with data calculated for the 2H-tautomer than with that of 1H-tetrazole (the SCF calculations were performed using PM3 method).[14] Much work has been done on the 5-substituted tetrazoles alkylation, and stereoselectivity of this reaction could serve as an indication as to point which tautomer is the reaction substrate. Nevertheless, interpretation of the data is a complex task because tetrazoles undergo the reaction in various ionic forms, not as neutral molecules.[1c,2,15] In the cases where the reaction conditions were such that the neutral 5-substituted tetrazoles reacted, the isomer alkylated in position 2 was predominant.[1c,d]

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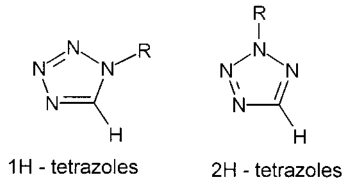

Figure 1. Tautomerism of tetrazole derivatives.

For 5-methyl-tetrazole Rażyńska et al.[3] have found the 2H-tautomeric form to occur in the gas phase. However, Butler et al.[16] have found that, in dioxane, the dominant form of 5-phenyl- and *p*-nitro-5-phenyltetrazoles is the 1H-tautomer (at percentages of 86 and 68, respectively). Sometimes the existence of only the 1H-tautomeric form is tacitly assumed even in the gas phase, as in the paper devoted to the calculation of heats of formation of many tetrazole derivatives by a semiempirical method[17] (six of them identical with those studied here). Once the energy difference between the two forms of 5C-tetrazole derivatives was calculated, the results have suggested the substituted molecules follow the same preference as that in the unsubstituted molecules. For example, calculations by Chen et al.[18] have shown several 5C-substituted 2H-tetrazoles to be more stable than the corresponding 1H-isomers. The same was true for azidotetrazoles[19] (substituted at either C or N), C-substituted nitrotetrazoles,[20] chlorotetrazoles,[21] and nitroaminotetrazoles.[22]

One objective of this work is to calculate energy differences for the tautomeric pairs of more tetrazole derivatives with a basis set larger than the one previously used, since the choice of basis set may account for variations in the energetic preference.[9,23] The second and main objective is to look for the reasons why the tautomeric preferences occur.

Our first step was to see whether the notion of aromaticity could help us account for the greater stability of 2H-tautomers of all the compounds investigated here. Reactivity of tetrazole and its 5-substituted derivatives permits to classify them as aromatic compounds; the ring undergoes electrophilic substitution[1b,c,2] and is stable toward oxidation.[1d,2] In general, the tetrazole ring remains unchanged during reduction of susceptible substituents.[1d]

Bird[24] has used the deviation from uniformity of the bond orders in aromatic rings to derive an index of aromaticity I_5 (for five-membered rings). A similar index, HOMA (harmonic oscillator measure of aromaticity) has been introduced by Kruszewski and Krygowski,[25] next adapted for heterocyclic π-electron systems.[26] Both indices and the minimum bond order in the ring, BO_{min}, were calculated and compared for the compounds investigated here. BO_{min} has been proposed by Jug[27] as another aromaticity index, whose magnitude corresponds to the weakest bond in the ring, which in turn sets an upper limit to the magnitude of the ring current.

In tetrazoles, two of the six π electrons required by the Hückel rule are provided by the "lone pair" of one nitrogen while the remaining four π electrons are provided by the other four atoms of the ring. Electronic delocalization is an important concept that can rationalize and predict the structural and electronic features of a variety of organic species. Now it is accepted that π electron delocalization is a byproduct of geometric constraints imposed by σ-electrons and not a driving force by itself. Shaik et al.[28] found that the σ electrons determine the regular hexagonal structure of benzene and that the π-electron delocalization must then be a byproduct phenomenon of the geometric constraints exerted by the σ frame. Jug and Köster[29] found that the π-electrons in the five-membered rings play a more important role in the structure determination than in the six-membered rings and that the equilibrium is closer to the localized structure than to the fully delocalized resonance structures.

Recently, Bean[30] has investigated delocalization and aromaticity in five-membered unsubstituted heteroaromatic compounds in terms of natural bond orbital (NBO) analysis because apart from giving the total charge on each atom it also separates the s- and p-electron densities and indicates the degree of electron delocalization measured as the depletion of bonding orbitals and the partial occupancy of "non-Lewis" antibonding NBOs. He found that the extent of transfer of electron density from the p_z orbital of the heteroatom to the rest of the π system (named by him the "n to π* transfer") is the best measure of delocalization and aromaticity of the compounds. He proposed an electronic aromaticity criterion, whereas otherwise generally three classes of aromaticity criteria have been considered: geometric (structural), energetic, and magnetic.[31,32]

Here NBO analysis was carried out in order to investigate the influence of substituents on the electron delocalization and, hopefully, to find a rationale for the larger stability of all derivatives of 2H-tetrazole. Recently, in the derivatives of imidazole, things were found to be different; some substituents stabilize the 1H-tautomers, whereas others stabilize 3H-tautomers.[33]

Computational Methods

Ab initio DFT wave functions and energies for each compound were calculated by using the 6-311++G** basis set, and with their geometries fully optimized. Similarly, NBO analysis[34] with the same basis set was performed. The calculations

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Table 1. Energies, Dipole Moments, Bond Lengths, and Geometric Aromaticity Indices of Substituted 1H-Tetrazoles

	R				
	BH_2	H	Br	Cl	CH_3
energy	−283.772307	−258.324257	−2831.858672	−717.938182	−297.658893
dipole moment	5.2696	5.7738	5.0586	4.9519	6.2344
d_{N1-N2}	1.3285	1.3511	1.3502	1.3511	1.3527
d_{N2-N3}	1.3063	1.2869	1.2885	1.2879	1.2864
d_{N3-N4}	1.3409	1.3631	1.3634	1.3630	1.3605
d_{N4-C5}	1.3365	1.3123	1.3086	1.3075	1.3174
d_{C5-N1}	1.3625	1.3462	1.3479	1.3473	1.3501
Bird's I_5	87.49	74.74	74.19	73.82	75.64
HOMA	0.939	0.834	0.833	0.829	0.8396
BO_{min}	1.491	1.432	1.430	1.432	1.443

	R				
	CN	NH_2	OCH_3	NO_2	F
energy	−350.577379	−313.705809	−372.886575	−462.865695	−357.581634
dipole moment	3.8839	6.4595	5.0937	3.4345	4.6665
d_{N1-N2}	1.3414	1.3678	1.3616	1.3384	1.3576
d_{N2-N3}	1.2916	1.2729	1.2821	1.2982	1.2863
d_{N3-N4}	1.3534	1.3622	1.3673	1.3559	1.3674
d_{N4-C5}	1.3202	1.3185	1.3127	1.3046	1.2968
d_{C5-N1}	1.3529	1.3497	1.3473	1.3427	1.3421
Bird's I_5	79.92	71.5	71.35	78.02	69.38
HOMA	0.888	0.784	0.788	0.882	0.782
BO_{min}	1.473	1.412	1.414	1.462	1.414

Table 2. Energies, Dipole Moments, Bond Lengths, and Geometric Aromaticity Indices of Substituted 2H-Tetrazoles

	R				
	BH_2	H	Br	Cl	CH_3
energy	−283.774271	−258.328896	−2831.863483	−717.943857	−297.663112
dipole moment	2.5610	2.2911	2.8045	2.9261	2.1397
d_{N1-N2}	1.3109	1.3264	1.3275	1.3276	1.3275
d_{N2-N3}	1.3416	1.3258	1.3244	1.3239	1.3228
d_{N3-N4}	1.2939	1.3071	1.3068	1.3069	1.3069
d_{N4-C5}	1.3768	1.3550	1.3546	1.3532	1.3611
d_{C5-N1}	1.3109	1.3259	1.3250	1.3244	1.3304
Bird's I_5	79.80	89.49	89.34	89.62	88.52
HOMA	0.918	0.969	0.970	0.971	0.966
BO_{min}	1.418	1.529	1.532	1.539	1.498

	R				
	CN	NH_2	OCH_3	NO_2	F
energy	−350.583581	−313.711580	−372.888076	−462.870483	−357.589990
dipole moment	5.1865	2.2381	0.3813	5.5882	3.2893
d_{N1-N2}	1.3190	1.3380	1.3319	1.3174	1.3306
d_{N2-N3}	1.3299	1.3162	1.3176	1.3336	1.3225
d_{N3-N4}	1.3001	1.3091	1.3121	1.3021	1.3104
d_{N4-C5}	1.3626	1.3620	1.3569	1.3471	1.3423
d_{C5-N1}	1.3312	1.3303	1.3290	1.3212	1.3174
Bird's I_5	86.57	87.27	89.90	88.76	89.88
HOMA	0.962	0.955	0.946	0.969	0.971
BO_{min}	1.490	1.493	1.520	1.559	1.572

were carried out by using Gaussian 98 programs.[35] Aromaticity indices I_5, HOMA, and BO_{min} were obtained by using the calculated bond lengths according to the expressions given in refs 24 (I_5 and BO_{min}) and 26 (HOMA).

Results

Tautomerism in Tetrazole Derivatives. To investigate this effect, the energies of 1H- and 2H-tetrazoles substituted at C5 were calculated at the B3LYP/6-311++G** level. The energies, as well as bond lengths inside the ring, are given in Tables 1 and 2. Tables 1 and 2 also list the geometric aromaticity indices for the compounds investigated, calculated on the basis of bond distances. Evidently, three indices (Tables 1 and 2) are larger for 2H-tetrazoles for all substituents, except for BH_2. Comparison of bond lengths of the shortest bonds in Tables 1 and 2 reveals that, except for BH_2 derivatives, they are always shorter in 1H- (d_{N2-N3}) than in 2H-tetrazoles (d_{N3-N4}). This tendency can be interpreted as a probe of the relative "diene character" or "bond fixation", which in turn may be considered a measure of the lack of aromaticity.[30]

Table 3 shows the relative energies of 2H- vs 1H-tautomers. It can be seen that, for all substituents, the 2H-tautomer is more stable than its 1H-counterpart.

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Table 3. Relative Energies of 1H- vs 2H-Tetrazole Derivatives in kcal/mol; R at the Ring Carbon Atom

	R									
	BH_2	H	Br	Cl	CH_3	CN	NH_2	OCH_3	NO_2	F
ΔE	1.23	2.91	3.02	3.56	2.65	3.89	3.62	0.94	3.00	5.24

Thus, comparison of the aromaticity indices can provide us with a strong indication toward the more stable tautomer but cannot be decisive in some cases. There must exist another factor (or factors) that is (or are) responsible for the energetic preferences. Since the indices studied here are based primarily on the distribution of bond lengths (Bird I_5 and BO_{min} use bond orders but they are calculated through bond lengths; HOMA is an exponential function of the bond length), we decided to look for the factors among the direct electronic properties of the species, calculated within the analysis of NBO (Tables 4 and 5). It is accepted that delocalization of electrons is invariantly connected with the aromatic character of the molecules,[32] expressed as their stability, more symmetric geometry, and other properties (e.g., propensity for electrophilic substitution), which are beyond the scope of this discussion.

The delocalization, especially in the molecules with heterocyclic rings, should result in a more uniform distribution of π electrons in the rings than it would have been without it. Bearing this in mind, we have calculated a standard deviation of the population of π electrons on the individual atoms in the tetrazole ring, SDn. The obtained values of SDn for tetrazole derivatives are given in Table 4 (1H) and Table 5 (2H). It can be seen that, for both derivatives, the SDn values are lower for the 2H- than for the 1H-tautomer. For 2H, the SDn values make 79−86% of those of 1H, except for the BH_2 derivative, for which the SDn difference between the two tautomers is lower (SDn for 2H being 91% of the SDn for 1H).

It follows that the π electron distribution around the ring is more uniform in the more stable tautomers. It is worth mentioning that the sum of all p_z natural orbital occupancies on atoms belonging to the five-membered tetrazole ring is very near to six; namely, it is in the range 5.90−6.08. One should also note that the SDn value calculated for a five-membered ring with two fully localized double bonds and a free electron pair on one heteroatom is equal to 0.4472 (values for tetrazoles in Tables 4 and 5 are about half of this figure).

Tables 4 and 5 also show some other electronic properties to be invariably higher for one tautomeric form than for the other: LP is the delocalization of the lone pair of trivalent (pyrrole-type) nitrogen atom, expressed as a difference between 2 and the calculated population of the p_z orbital on N1 in 1H-tetrazoles and on N2 in 2H-tetrazoles. The "% non-Lewis" is the portion of the electron density delocalized in the antibonding orbitals. This delocalization is partially due to the transfer of π electrons from the two double bonds of the Lewis structure to the two π^* orbitals (π to π^*) and partially to the transfer of electron density from the p_z orbital of trivalent (pyrrole-type) nitrogen atom to the two π^* orbitals (n to π^*).[30] Another measure of delocalization, apart from the "non-Lewis", is the population of two antibonding π^* orbitals, BD*, included in Tables 4 and 5. The magnitude of BD* amounts to 30−60% of the total delocalization; the rest of the delocalized electron density is placed into other antibonding orbitals. These properties are lower for all 1H- than for 2H-derivatives. LP is equal to 0.35−0.46 and 0.46−0.49 in 1H- and 2H-tetrazoles, respectively.

We have investigated the relations between these electronic properties by regressing linearly one to the other for the group of all 1H- and 2H-tautomers. The highest correlation coefficient was found for the regression of LP vs SDn: it was equal −0.895. This result means that the higher the degree of delocalization of the lone pair on N1/N2, the more even the distribution of the π-electron population.

Bean[30] found that the extent of the transfer of electron density from the p_z orbital of the heteroatom to the rest of the π system is the best masure of delocalization and aromaticity of a class of five-membered compounds. We suppose that the same parameter can serve as an electronic criterion of aromaticity for the class of compounds investigated here. What is more, other electronic parameters, calculated with the NBO procedure, can also serve as such. For the group of 20 1H- and 2H-tautomers, the geometric and electronic properties are well correlated, e.g., correlation coefficients of HOMA against SDn, LP, and BD* equal to −0.820, 0.973, and 0.902, respectively. Even better correlation was obtained after regressing the differences between the corresponding values (2H−1H): the correlation coefficient for regressing ΔHOMA against ΔLP, ΔSDn, Δ% non-Lewis, and ΔBD* were equal to 0.921, −0.941, 0.915, and 0.982, respectively. This fact exemplifies the intermingling of the nuclear and electronic coordinates.

The proposition that the smaller stability of 1H- vs 2H-derivatives is parallel to the more aromatic character of the latter ought to be validated by comparison of other criteria of aromaticity of the compounds, reflecting different physicochemical properties. The characteristics chosen (according to the referee's suggestion) were a magnetic property—the nucleus independent chemical shift (NICS),[36] and the energetic characteristics—the aromatic stabilization energy (ASE),[37,38] calculated as the energetic effect of an imaginary homodesmic reaction (eq 1); the calculated NICS and ASE values are given in Tables 6 and 7. Clearly, calculation of these additional criteria of aromaticity is the more desirable as it was recently found that aromaticity is a multidimensional phenomenon, at least for the heterogeneous groups of compounds, e.g. heteroaromatics in which the number of heteroatoms varies. The NICS and ASE characteristics correlate quite well with the geometric and electronic

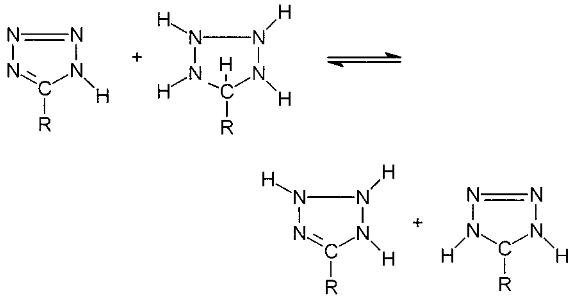

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Table 4. NBO Results for Substituted 1H-Tetrazoles

	R									
	BH_2	H	Br	Cl	CH_3	CN	NH_2	OCH_3	NO_2	F
charge on R	0.3291	0.2056	0.1580	0.0757	0.0686	0.0084	−0.0531	−0.2030	−0.2250	−0.3405
lone pair on N1	0.4593	0.4014	0.4006	0.3956	0.3941	0.4281	0.3458	0.3544	0.4417	0.3700
SDn	0.2127	0.2601	0.2430	0.2467	0.2719	0.2251	0.3064	0.3031	0.2156	0.2813
% non-Lewis	2.262	2.108	1.199	1.620	1.819	1.889	1.865	1.623	2.533	1.793
BD*	0.7166	0.6188	0.6601	0.6618	0.6318	0.6787	0.6567	0.6429	0.6750	0.6189

Table 5. NBO Results for Substituted 2H-Tetrazoles

	R									
	BH_2	H	Br	Cl	CH_3	CN	NH_2	OCH_3	NO_2	F
charge on R	0.3259	0.1984	0.1422	0.0621	0.0601	0.0011	−0.0615	−0.2193	−0.2298	−0.3485
lone pair on N2	0.4802	0.4746	0.4752	0.4752	0.4735	0.4856	0.4636	0.4813	0.4885	0.4755
SDn	0.1934	0.2123	0.1974	0.1995	0.2214	0.1883	0.2522	0.2380	0.1849	0.2267
% non-Lewis	2.316	2.519	1.418	1.929	2.178	2.098	2.306	2.076	2.785	2.264
BD*	0.7361	0.7664	0.8157	0.8238	0.7888	0.7812	0.8549	0.8728	0.7796	0.8232

Table 6. Aromatic Stabilization Energy (ASE, kcal/mol) and GIAO-SCF Nuclear Independent Chemical Shift (NICSs, ppm) of Substituted 1H-Tetrazoles

	R									
	BH_2	H	Br	Cl	CH_3	CN	NH_2	OCH_3	NO_2	F
ASE	16.30	14.48	7.06	7.18	13.34	15.09	6.82	7.99	7.23	5.67
NICS	−13.05	−14.34	−12.06	−11.91	−12.72	−14.30	−11.50	−11.07	−12.01	−11.32

Table 7. Aromatic Stabilization Energy (ASE, kcal/mol) and Nuclear Independent Chemical Shift (NICSs, ppm) of Substituted 2H-Tetrazoles

	R									
	BH_2	H	Br	Cl	CH_3	CN	NH_2	OCH_3	NO_2	F
ASE	23.17	23.06	27.80	28.46	21.86	25.77	20.40	23.13	25.40	27.45
NICS	−13.44	−14.47	−13.20	−13.16	−13.35	−14.52	−12.23	−12.90	−13.75	−13.38

ones: correlation coefficients of regression of NICS with SDn and LP are 0.685, and −0.667; ASE with SDn and LP are −0.730 and 0.882, respectively. Correlation of the third electronic characteristics, BD*, with NICS was poor (−0.366) but it was rather good with ASE (0.852).

The relationships exhibited in the data are frequently treated by principal component analysis (PCA). Using this analysis, Katritzky et al.[32] found that some concepts of aromaticity, named by them as “classical”, and others, named “magnetic”, are almost completely orthogonal. Presently, we have performed a similar analysis including substituted 1H- and 2H-tetrazoles mentioned in Tables 1 and 2. The set of characteristics consists of three geometric (Tables 1 and 2), three electronic properties (Tables 4 and 5), one energetic (ASE) and one magnetic (NICS) aromaticity criterion (Tables 6 and 7). The PC loadings for a group of all 20 compounds (1H- and 2H-tetrazoles) are presented in Figure 2. The lines that intersect at (0,0) represent the input variables. The length of each vector is proportional to its contribution to PC. It reflects how each variable weighs the two components. The angle between any two component lines is inversely proportional to the correlation between them.[39] It was found that 92% of the variation of characteristics was explained by the two principal components, for which the first and second accounted for 82% and 10% of the variance, respectively. The figure shows that all characteristics have similar PC1 loadings but markedly differ in PC2. All of the variables except SDn and NICS positively weigh component 1. Component 2 is heavily weighed by the variable NICS. Some of the properties are almost orthogonal to each other in the meaning applied by Katritzky, and aromaticity described by the criteria mentioned above has to be considered as a multidimensional one, indeed, even for such a homogeneous group of compounds.

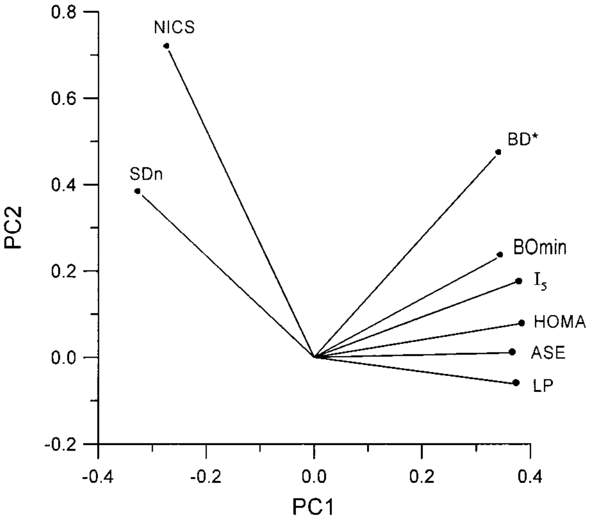

Figure 2. Various aromaticity indices in two-dimensional principal component space for 1H and 2H 5C-substituted tetrazoles.

Nevertheless, inspection of Tables 6 and 7 reveals that for all of the derivatives under study, the values of ASE and the values of NICS are higher for 2H- than for 1H-tetrazoles. Because the same was true for all of the electronic properties contained in Tables 4 and 5, one can

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[39] *Statgraphics*, version 5; STSC, Inc. 2115 East Jefferson Street, Rockville, MD 20852.

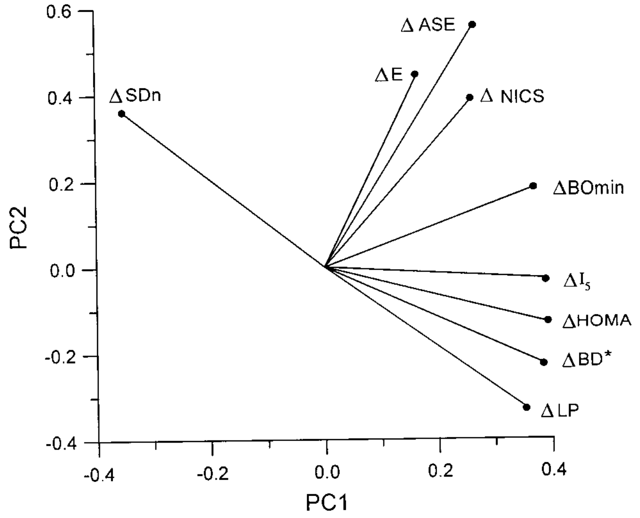

Figure 3. Principal component analysis of the set of variables representing increments of aromaticity criteria (the same as in Figure 2) and increment of energy (2H − 1H) for 5C-substituted tetrazoles.

say that according to ASE, NICS, and electronic criteria, 2H-tautomers are more aromatic than their 1H-counterparts.

Similar PCA was made for the difference (2H − 1H) of the same set of characteristics. The result is given in Figure 3. In this case the first two principal components explained only 85.3% of variance; yet 10% was comprised in the third principal component. According to Katritzky's interpretation of PCA analysis, ΔE is almost orthogonal to ΔI_5 and ΔHOMA. ΔE is relatively near to ΔNICS in the plane spanned on PC1 and PC2, but the correlation is very poor (0.157) as a result of the fact that both values strongly load PC3, which is not visible on the plane. A slightly better (but still poor) correlation is found for ΔE and ΔI_5 (0.438), and for ΔE and ΔASE (0.438).

According to Wong et al.,[40] conformations with no dipole moments are usually preferred to those leading to dipoles, for electrostatic effects are often important in the gas phase. In the hope that perhaps the energetic preference in the tautomeric pairs would favor the tautomer having the lower dipole moment, dipole moments of the tautomers were also compared. Still, the correlation coefficient was no better (−0.408).

It can be seen that no single property can explain the energy difference (2H − 1H) quantitatively.

According to Butler,[16] the tetrazole ring is invariably planar with bond lengths characteristic of an aromatic system. Nevertheless, the calculations display that in 2H-tetrazole and both 5C-aminotetrazoles the tetrazole ring is not rigorously flat. Evidently, this slight deviation from flatness has no influence on the aromaticity as measured by geometric and electronic criteria, and 2H-tetrazole is more aromatic than the 1H-tautomer.

It may also be of interest that, for tetrazoles substituted at C5 by OH and SH groups, 2H-tautomers have lower energies than 1H- and are more aromatic according to HOMA and I_5 indices. The electronic properties show the same tendency as evident in the other compounds placed in Tables 4 and 5. Nevertheless, these derivatives were not included in the tables because the energy calculated for the keto form of the OH and SH derivatives was much lower than that of the four enol tautomers; one can presume that the keto form is the predominant species in the gas phase and in the solutions.

NBO Substituent Charges vs Their Electronegativity. In Tables 1−5 the compounds are ordered according to the increasing negative charge on substituent R in 1H-derivatives (Table 4). In Tables 1 and 2 the ordering of tetrazole substituents according to their charge is compared with the atom and group electronegativities, as determined by Boyd et al.,[41,42] who used the bond critical point model. The bond connected the atom/group under interest with hydrogen. Boyd's electronegativities arranged in the increasing order are BH_2 (1.92) < CH_3 (2.55) < CN (2.69) < Br (2.75) < Cl (3.05) < NH_2 (3.12) < NO_2 (3.22) < OCH_3 (3.53) < F (4). In 1H-tetrazoles the ordering of substituents is different: CH_3 and CN groups are less positive than in the Boyd arrangement, and OCH_3 is less negative than NO_2. One interesting question emerges from that comparison: is the difference due to the fact that Boyd's results were obtained by using the atoms-in-molecules (AIM) theory, whereas for the present calculations the NBO analysis was applied, or is the difference due to different references used?

Boyd has calculated the properties of the bond AH (where A is the group of interest), and we have investigated charge of A connected to the tetrazole ring. Further work is currently under way to find a satisfactory answer to the question.

Influence of Substituents on the Aromaticity of Two Tautomeric Forms. There can arise the question of how the individual substituent influences the aromaticity of tetrazole. We attempted to answer this question separately for both tautomers. To this purpose, the PCA was applied using the same set of characteristics as for the construction of Figure 3. The conclusions are consistent with those that can be drawn by inspection of Tables 1, 2, and 4−7. For both tautomers the influence of substituents on aromaticity was different and depended strongly on the type of characteristics used for the evaluation. For 1H-tautomers, the most aromatic derivatives according to ASE and NICS are CN- and H-derivatives; according to SDN they are NO_2- and BH_2-; and according to LP and geometric indices it is the BH_2-. In the group of 2H-tautomers, according to ASE they are Br-, Cl-, and F-; according to NICS they are H- and CN-; according to LP and SDn they are CN and NO_2-, according to I_5 they are OCH_3- and F-, and according to HOMA they are F- and Cl-substituted derivatives. On the basis of PCA maps, one can select H-, CN-, and BH_2- as the "most aromatic" in the first group, and NO_2-, CN-, and F-substituted derivatives in the second group.

It can be seen that the one-dimensional ordering is not possible. Hence, the multidimensionality of the aromaticity notion[32,38,43,44] is manifested in this case.

Conclusions

Calculations of the energy of 10 tetrazole C5-derivatives carried out by the DFT method at the B3LYP/6-311++G** level showed that 2H- are more stable than

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1H-tautomers. The aromaticity indices, expressed through bond lengths, were lower for all 1H- than for 2H-tautomers, except for BH_2-tetrazole. On the other hand, the electronic parameters point at a larger electron delocalization of 2H-tautomers in all cases. The same is true for a magnetic parameter, NICS, and an aromatic stabilization energy, ASE.

A new measure has been suggested to describe electron delocalization, viz., root-mean-square of p_z electron density on all atoms belonging to the five-memebered tetrazole ring, SDn. It is correlated with the extent of the transfer of electron density from the p_z orbital of the trivalent (pyrrole-type) nitrogen atom to the rest of the π system, LP (the parameter very similar to Bean's "n to π^* transfer", which was found to describe best the aromaticity in a series of five-membered heteroaromatic compounds[30]). The differences of SDn are well correlated with the differences of the HOMA aromaticity index for 2H- and 1H-derivatives. SDn can serve as a new aromaticity index, based on the explicit electronic properties of the system, together with LP and BD* (population of the two antibonding π^* orbitals). Principal component analysis showed orthogonality of some pairs of aromaticity criteria (especially the magnetic (NICS) and the electronic (BD*) ones), but all of the NBO electronic parameters, NICS, and ASE were larger for 2H- than for 1H-tetrazoles.

Investigation of the influence of the individual substituents on aromaticity, conducted separately for the series of 1H- and 2H-tautomers, showed that the property can be treated as multidimensional, since according to different aromaticity criteria different compounds could be evaluated as the most aromatic.

Acknowledgment. I am grateful to my reviewers for careful and constructive criticism.

Supporting Information Available: Z-matrices, geometrical parameters and energies for 20 tetrazole derivatives. This material is available free of charge via the Internet at http://pubs.acs.org.

JO010062N