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Electric Field Gradient for Prediction of Effect of Cation Na^+ on Nucleic Acid Bases, Aromaticity by Cyclic References

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ABSTRACT

In this research, effects of Na+ ion on Nitrogenous Organic Bases (NOB) in the nucleic acids by using of a new index. This index is according to Electric Field Gradient (EFG) in the middle of bond and evaluated as a reference by corresponding cyclic same compounds. The studied molecules were Adenine, Guanine, Cytosine, Thymine and Uracil that has been investigated. The trend of changes of aromaticity by putting Na+ in the middle of cycle and change of distance according to degree of Angstrom (Å). It has been used Density Functional Theory (DFT) as a method for geometrical optimization Beck 3 Lee Yang Parr (B3LYP) in 6-311++G** and 6-31G standard basis set. These calculations have been done in two steps. In the first step, it has been calculated electric field gradient in the middle of bond in absence of Na+ (EFG0) and in the second step in presence of Na+, it has been calculated in 1Å distance of middle of bond without Na+ (EFG0.5) and with Na+ that compared amount of aromaticity between EFG0 and EFG0.5 in 6 distance (d = 0.5, 1, 1.5, 2, 2.5 and 3 Å).

Keywords: Nucleic Acid; Na^+; Electric field gradient (EFG)

1. Introduction

In molecular biology, two nucleotides on opposite complementary deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), strands that are connected via hydrogen bonds are called a base. DNA and RNA were first isolated by the Swiss physician Friedrich Miescher who, in

1869, discovered a microscopic substance in the pus of discarded surgical bandages. As it resided in the nuclei of cells, he called it "nuclein". In the canonical Watson-Crick DNA base pairing, adenine (A) forms a base pair with thymine (T) and guanine (G) with cytosine (C). In RNA, thymine is replaced by uracil (U) [1]. Uracil ($C_4H_4N_2O_2$) is a common and naturally occurring pyrimidine derivative. Uracil [Pyrimidine-2,4(1*H*,3*H*)-dione] undergoes amide-imidic acid tautomeric shifts because any nuclear instability the molecule may have from the lack of formal aromaticity is compensated by the cyclic-amidic stability. The amide tautomer is referred to as the lactam structure, while the imidic acid tautomer is referred to as the lactim structure [2].

Aromaticity is a chemical property in which a conjugated ring of unsaturated bonds, lone pairs, or empty orbitals exhibit a stabilization stronger than would be expected by the stabilization of conjugation alone. This property led to the term "aromatic" for this class of compounds, and hence the term "aromaticity" for the eventuallydiscovered electronic property. The circulating π electrons in an aromatic molecule produce ring currents that oppose the applied magnetic field in NMR. The NMR signals of protons in the plane of an aromatic ring are shifted substantially further down-field than those on non-aromatic sp^2 carbons. This is an important way of detecting aromaticity [3]. Aromatic molecules are able to interact with each other in so-called π-π stacking: the π systems form two parallel rings overlap in a "face-toface" orientation and interact with each other in an "edgeto- face" orientation: the slight positive charge of the substituents on the ring atoms of one molecule are attracted to the slight negative charge of the aromatic system on another molecule. An atom in an aromatic system can have other electrons that are not part of the system, and are therefore ignored for the $4n + 2$ rule. Uracil that make up the sequence of the genetic code in RNA is aromatic pyrimidine. Considering that aromaticity is a multidimensional phenomenon, the investigation of new aromaticity indicesis very important. In this sense, it has been introduced the corrected total electron density (CTED) as an index of aromaticity based on ellipticity (ε) and bond length variations from those for a system assumed as full aromatic. The validity of this index was checked for a series of rings in monocyclicand polycyclic structures. Also, the aromaticity of polycyclic benzene rings was evaluated from the calculation of the average g-factor for a hydrogen placed perpendicularly at geometrical center of related ring plane at a distance of 1.2˚A. The results have been compared with the other commonly used aromatic indices, such as HOMA, NICSs, PDI, FLU, MCI and CTED [4].

2. Experimental

Computational Details

All the compounds have been fully optimized energies at equilibrium geometries by using DFT at B3LYP level with 6-311++G** [5] basis set. Frequency test has been done to ensure that all the optimized geometries are in ground state. The optimized geometries show that all rings are planar (in xy plane). The EFG calculations at the sites of atoms and in the middle and above the bonds have been made according to the procedure (see Results and discussion below) for optimized structures. The calculations have been done by Gaussian09 [6] package.

3. Results and discussion

In atomic, molecular, and solid-state physics, EFG measures the rate of change of the electric field at an atomic nucleus generated by the electronic charge distribution and the other nuclei. The electric field gradient tensor, Vij, which is defined by the second derivatives of the potential generated by electron density with respect to desired position of molecule, is a useful tool to obtain some molecular information. The electric field gradient tensor is a symmetric second rank tensor with zero off diagonal elements which can be expressed in an axis system. This component has been assigned to “EFG” in this manuscript. The unit of computed EFG value is Volt per square meter (Vm-2 or NC-1 m-1)[7].

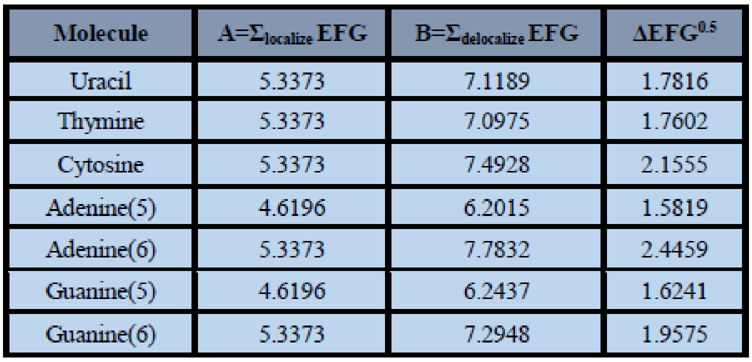
In this research, to finding compounds in their cyclic form have four kinds of bonds such as: C=C, C-C, C-N, C=N. So, it has been selected two cyclic references that have localized electrons in bonds named cyclohexene and 1, 2, 5, 6-tetra hydro pyrimidine [8].

By using of a new index of corresponding amount of aromaticity (electric field gradient) in two steps amount of aromaticity in NOB in DNA and RNA has been calculated. We have calculated amount of aromaticity in NOB being in the Nucleic acids without Na+ ion by using EFG. That style of putting Bq in the cycle has been observed in fig 1and amount of aromaticity of seven styles has been shown in Table 1. Na+ ion has been located in 0.5, 1, 1.5, 2, 2.5 and 3 A° distances of middle of cycle and according to this, aromaticity of NOB has been calculated. Style of putting Na^+ ion has been shown in Fig1. The amount of aromaticity of seven cycles has been listed in table 1 and 2.

The EFG is non-zero only if the charges surrounding the nucleus violate cubic symmetry and therefore generate an inhomogeneous electric field at the position of the nucleus. EFGs are highly sensitive to the electronic density in the immediate vicinity of a nucleus. This is because the EFG operator scales as $r-3$, where r is the distance from a nucleus. This sensitivity has been used to study effects on charge distribution resulting from substitution, weak interactions, and charge transfer. A=Σlocalized EFG is sum of references EFG, B=Σdelocalized EFG is sum of Eigen values in vzz and $\Delta = B - A$ is aromaticity amount of uracil as an example of these molecules

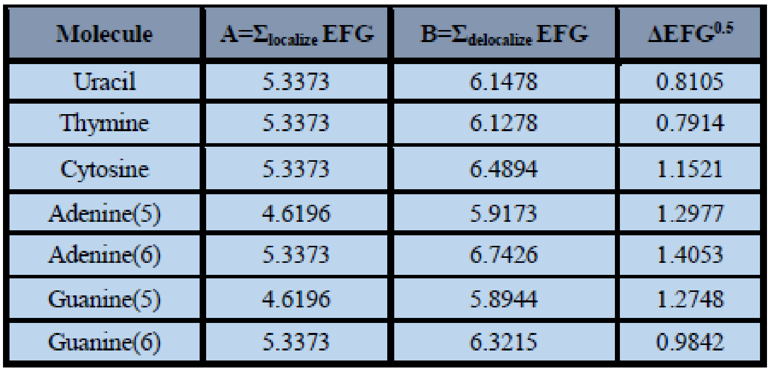
Fig. 1: Uracil molecule with cation

By putting Na^+ ion in the middle of cycle according to different distances of studied 7 cycles. Whenever Na^+ ion localized in 3A distance is stable structure than other and whenever Na^+ ion localized in 0.5 A distance is unstable structure than other.



Molecule	$A=\Sigma_{localize}$ EFG	$B=\Sigma_{delocalize}$ EFG	$\Delta EFG^{0.5}$
Uracil	5.3373	7.1189	1.7816
Thymine	5.3373	7.0975	1.7602
Cytosine	5.3373	7.4928	2.1555
Adenine(5)	4.6196	6.2015	1.5819
Adenine(6)	5.3373	7.7832	2.4459
Guanine(5)	4.6196	6.2437	1.6241
Guanine(6)	5.3373	7.2948	1.9575

Table 1: The amount of aromaticity without Na^+



Molecule	$A=\Sigma_{localize}$ EFG	$B=\Sigma_{delocalize}$ EFG	$\Delta EFG^{0.5}$
Uracil	5.3373	6.1478	0.8105
Thymine	5.3373	6.1278	0.7914
Cytosine	5.3373	6.4894	1.1521
Adenine(5)	4.6196	5.9173	1.2977
Adenine(6)	5.3373	6.7426	1.4053
Guanine(5)	4.6196	5.8944	1.2748
Guanine(6)	5.3373	6.3215	0.9842

Table 2. The amount of aromaticity with Na^+

Amount of aromaticity in this 7 cycle calculated by EFG in the middle of bond (ΔEFG0) and in 0.5 and 1 *A*0 have the same trends. So, standard test of EFG has been determined for cycles in 0.5 A distance of bond. Results show by entrance of Na+ ion, amount of aromaticity of compounds has been reduced as seen in Table 2. Whatever distance of it get away from cycle, amount of aromaticity of compounds has been increased.

So, the trend of changes of stablity from these compounds is such as below:

Without Na+ > 3 > 2.5 > 2 > 1.5 > 1 > 0.5

The amounts of aromaticity in these compounds have been calculated in some different distances of cations. The results have shown the same trends such as in 1 *A*0 by EFG0.5 at different distances 0.5, 1,1.5, 2, 2.5, 3 *A*0 (Fig 2).

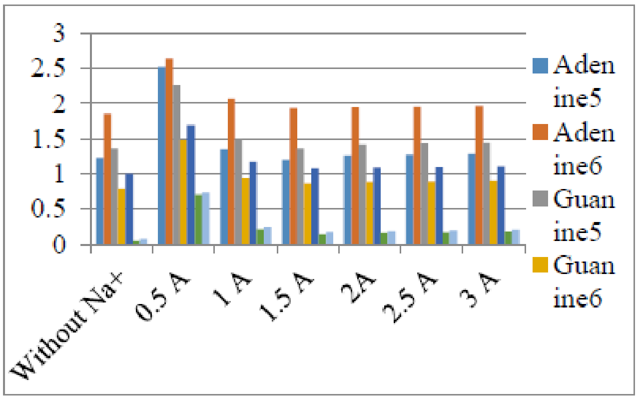


Fig 2: The comparison of aromaticity of different distances of Na$_{+}$ in EFG$_{0}$

Also, hexa-membered cycles show that in both standard in EFG0 and EFG0.5 and EFG1 and have similar trend. Adenine, cytosine, tymine, and uracil have more aromaticity. The trend of changes of aromaticity in 5 cycles investigated and all of them have same trend that in contrast this trend with other standard of aromaticity like NICS and HOMA has been showed good adaptation. So, we have found from trends of changes of aromaticity, when EFG on bond in 0.5 A distance changes, amount of aromaticity in more distances increases.

4. Conclusions

Several nitrogenous Organic Bases have been optimized at B3LYP/6-311++G** level of theory with no imaginary frequencies. All the rings which have been optimized are planar. Electric field gradient EFG calculations have been performed for these species and presented a new criterion for aromaticity, which are indicated by ΔEFG. Positive ΔEFG values indicate the presence of aromaticity, whereas negative values denote anti aromaticity. Our method is computationally much easier and inexpensive to compute. Since EFG calculations are used the most in some other quantum mechanical programs, this type of aromaticity evaluations will be readily available.

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