

A Theoretical Study on the Aromaticity of 5-methylcytosine tautomers in the gas phase

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ABSTRACT

The aromaticity of 5 methylcytosine tautomers in the gas phase has been studied and the chemical structures of related tautomers are investigated . The electronic energy, enthalpy and free energy of each tautomer are also estimated at the B3LYP/6-31 G* // B3LYP/6-31 G* and MP2 / 6-31 G* // MP2 / 6-31 G* Levels .

Keywords: Aromaticity; Tautomer; Enthalpy; Free energy

INTRODUCTION

The aromaticity is an important parameter used frequently as a measure of reactivity of many organic and even some inorganic molecules [1]. About 50% of all known organic compounds may be characterized by more or less pronounced aromatic characters. This is especially important for heterocyclic compounds since this class comprises many species of great biological importance such as porphyrins and nucleic acid bases. Many theoretical criteria for aromaticity have been proposed but three of them have proven to be

The most useful. They address aromaticity to energetic [2–4], geometric [5–10] or magnetic properties [11–16]. Resonance energy was the first quantitative measure of aromatic character [2] and still provides useful characteristics of aromaticity.

Magnetic properties of organic molecules arise from the diamagnetic ring currents of aromatic systems. The nucleus independent chemical shift (NICS) was defined by Schleyer et al. [11] as a negative value of the absolute magnetic shielding computed in centers of ring or 1 Å

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The molecular plane. NICS at an empty point in space equals to zero and in principle does not require reference molecules and calibrating (homodesmotic) equations for evaluation of aromaticity. Negative values of NICS indicate shielding—presence of induced diatropic ring currents understood as aromaticity at specific point. On the contrary, its positive values are interpreted as deshielded—paratropic ring currents and antiaromaticity. Schleyer et al. [12] after studies on an extensive set of heterocyclic compounds, proved that there are very good linear correlations between geometric, energetic, and magnetic properties providing straightforward interpretation of the electronic structures and properties of organic molecules. Despite the fact that it is not obvious localization of maximum shielding, distance of 1 Å above the molecule geometric center is commonly accepted as a reference point. Such value denoted as NICS(1) is then a measure of aromaticity [11–16].

METHODS OF CALCULATIONS

All structures relate to 5-methylcytosine were fully optimized using hybrid Becke 3 Lee–Yang–Perdew (B3LYP) [18,19] gradient-corrected approximation within density functional theory B3LYP/6-31G* and second level Moller-Plesset perturbation theory MP2/6-31G* without any geometrical restrictions. It is to be the standard for this kind of calculations [13,17]. The geometries were checked whether they correspond to global minimum based on subsequent second energy gradients matrix analysis. All of the optimized structures have only positive force constants which indicate location on the global minimum on PES. Besides, Gauge invariant atomic orbitals (GIAO) method was applied to estimate the magnetic tensor shielding within the same level of approximation (B3LYP/6-31G* and MP2/6-31G*). For all studied tautomers, the sets of points laying below and above rings geometric centers were used. Their locations correspond to distances from -3.5 to 3.5 Å with 0.5 Å step. All calculations were performed based on GAUSSIAN 03 program [20].

RESULTS AND DISCUSSION

Analyzing the results reveals that the most important tautomerism is the keto-amino/enol. The chemical structures of these four tautomers are shown in Fig. 1. Table 1 shows the electronic energy, enthalpy and free energy of each tautomer in the gas phase that are estimated at the B3LYP/6-31G*//B3LYP/6-31G* and MP2/6-31G*//MP2/6-31G* levels.

The measure of aromaticity of each studied tautomer was characterized on the basis of magnetic properties. Figs. 2 and 3 characterize aromaticity of four stable tautomers of 5-methylcytosine. Additionally, benzene was used as a reference molecule: it is obvious aromaticity reference points for six-member rings. The plots of Fig. 2 and 3 allow for location of aromaticity maximum of studied tautomers, direct comparison and relation to the reference molecule. Since NICS, plots of all tautomers are symmetrical along with molecular plane, the only above plane points were presented in Figs. 2 and 3. This feature is rather expected due to ring planarity and insignificant influence on magnetic shielding of nonplanar side groups. The minimum of NICS is located in the range of 0.5–1.5 Å below and above the plane. Despite to this, data related to 1.0 Å separation of molecular plane will be used in further discussion regarding the common acceptance of such distance as the reference point of aromaticity [12].

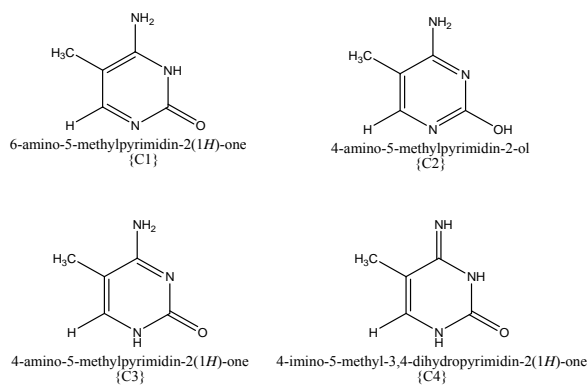


Fig.1. Molecular scheme of four investigated tautomers.

Table 1. Electronic energy, enthalpy and free energy (in Hartree) of investigated tautomers of 5-methylcytosine in the gas phase

#	LEVEL	C1	C2	C3	C4
Electronic energy(E)	MP2	-432.9246843	-432.9381103	-432.9365773	-432.9349222
	DFT	-434.2351629	-434.2447220	-434.2460806	-434.2432367
Enthalpy (H)	MP2	-432.794304	-432.807606	-432.805922	-432.804350
	DFT	-434.104090	-434.113354	-434.114678	-434.111577
Free energy (G)	MP2	-432.837068	-432.849333	-432.848090	-432.846865
	DFT	-434.146423	-434.154893	-434.156649	-434.153506

Systems with negative NICS values are aromatic, since negative values obtain when diatropic ring current (shielding) dominates, whereas systems with positive values are antiaromatic because positive values arise when paratropic current (deshielding) dominates. The NICS 0 Å values calculated at the centre of the ring are influenced by σ -bonds, whereas the NICS 1 Å values calculated at 1 Å out of the plane are more affected by the π -system.

Comparing four tautomers of 5-methylcytosine to benzene as a reference (contain six-member ring) allows for direct comparison of their aromatic features. From Fig. 2 and 3, one may conclude that all tautomers are less aromatic compared to benzene. All tautomers exhibit a significant decrease of NICS value from point located in the geometric center of the ring to 0.5 Å above or below. This stands for existence of delocalized π -electron current above and below the molecular planes as expected for aromatic compounds. The strongest aromatic character has been found for C2. C1 is also characterized by significant relative aromaticity, but lower compared to C2. C3 has been identified as third tautomer with respect to its aromaticity. This molecule should be classified as moderate aromatic compound and at distance of 1 Å from heterocyclic plane is characterized by NICS(1) about 32-39% of the value of one corresponding to benzene.

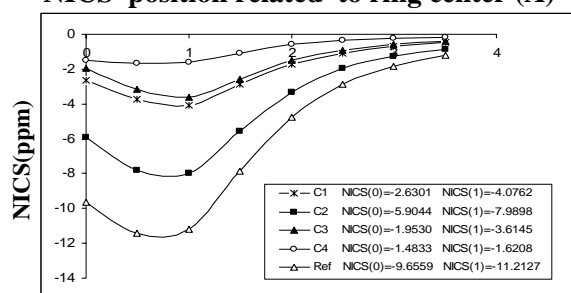
NICS position related to ring center (Å)

Fig.2. Aromaticity of 5 - methylcytosine tautomers estimated as a function of NICS (negative value of magnetic tensor shielding) versus atomic distance from ring geometric center with B3LYP/6-31G* method. NICS(0) and NICS(1) denote values estimated at ring geometric center and 1 Å above the plane respectively.

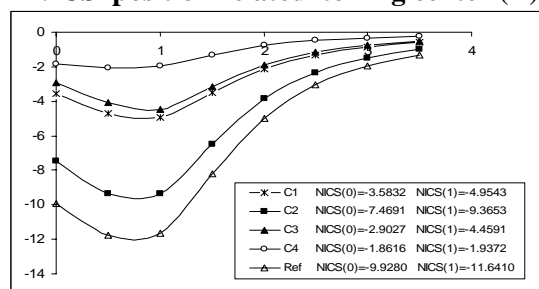
NICS position related to ring center (Å)

Fig.3. Aromaticity of 5 - methylcytosine tautomers estimated as a function of NICS (negative value of magnetic tensor shielding) versus the distance from ring geometric center with MP2/6-31G* method. NICS(0) and NICS(1) denote values estimated at ring geometric center and 1 Å above the plane, respectively.

CONCLUSION

The results of our calculations lead to the conclusion that nucleic acid bases are compounds of diverse aromatic character. C2 is significantly more aromatic compared to the other tautomers (see Fig.1).

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