

An ab initio study of electronic Structure and properties of guanosine

Dr. Sanjay Kumar Mishra

Department of Applied Science and Humanities
I.T.S Engineering College
Greater Noida, India
skmishraphy@its.edu.in

Dr. Nidhi Puri

Department of Applied Science and Humanities
I.T.S Engineering College
Greater Noida, India
nidhipuri.ash@its.edu.in

Abstract— Ground state geometries of the two tautomeric forms of guanosine (rG) of anti-conformations of keto-N9R and keto-N7R, R=sugar moiety in rG were optimized using the ab initio at B3LYP6-31G** level. These calculations were also extended to hydrogen-bonded complex of two water molecules with each of the keto-N9R (rG9-2W) and keto-N7R (rG7-2W) forms of rG. Relative stabilities of the two above mentioned tautomers of rG as well as those of rG-2W (keto-N9R) and rG-2W (keto-N7R) complexes in the ground state in the gas phase were studied employing the MP2 correlation correction. It appears that both the keto-N9R and keto-N7R forms of rG would be present in the ground state, particularly near the aqueous solution-air interface.

Keywords: Guanosine (rG); Ab initio study; Tautomerism

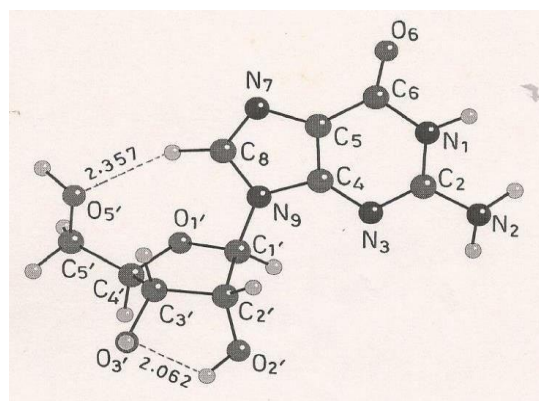
I. INTRODUCTION

Guanosine (rG) is a purine nucleoside comprising guanine attached to ribose ring and an important building block for supramolecular gels owing to the unique self-assembly property that results from the unique hydrogen-bond acceptors and donor groups [1]. Mutation of biological systems and carcinogenesis are complex phenomena involving genetic changes at the molecular level which are not yet properly understood. Incorporation of enol and imine tautomers of the bases in the nucleic acids in place of normal keto and amino forms respectively is considered to be one of the different possible causes of mutation [2,3]. However, theoretical studies suggest that the enol and imine tautomers of the bases may not occur abundantly enough to be important for mutation [4,5]. A bottleneck in the study of tautomers is the fact that these species are normally not crystallized. However, in this context, spectroscopic and theoretical methods appear to be quite useful [4-7]. Electronic absorption, fluorescence and ab initio quantum theoretical calculations have shown that the guanine base of the nucleic acids mainly in the keto-N9H form inside bulk water while it occurs in the keto-N7H form at the water-air interface [5]. In an experiment study using hole burning spectroscopy [8], beside the keto-N9H and keto-N7H forms, an enol tautomer of guanine was also found to occur. These results give rise to important questions as what would be the relative stabilities of the keto-N9R and keto-N7R tautomeric forms of rG, where R stands for the sugar moiety, in bulk water and at the water-air interface. However, to the best of our information, the possibility of occurrence of the keto-N7R form of rG in gas phase and aqueous media has not

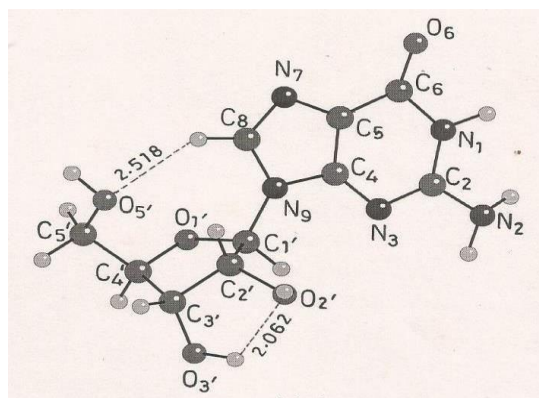
yet been studied.

II. METHOD OF CALCULATIONS

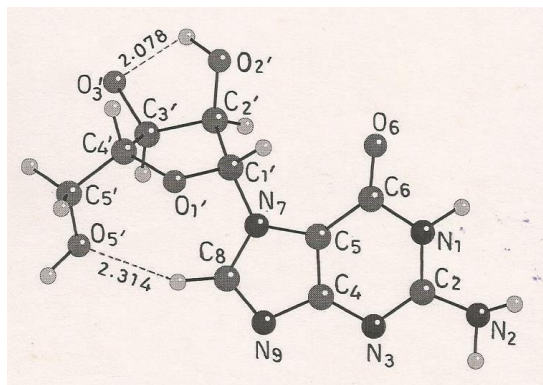
Molecular geometries of the anti-conformation of the two tautomeric forms of rG (keto-N9R and keto-N7R, R=sugar moiety in rG) and anti-conformations of keto-N9R and keto-N7R forms of rG-2W (Figs. 1, 2) were optimized using the ab initio at B3LYP/6-31G** level [5]. Due to a large size of the molecule and as a detailed investigation of its two tautomeric forms in both gas phase and aqueous media was undertaken, a more sophisticated basis set could not be employed. All these calculations were performed using Windows version of Gaussian 94 (G94W) (Revision E.3) program [9].



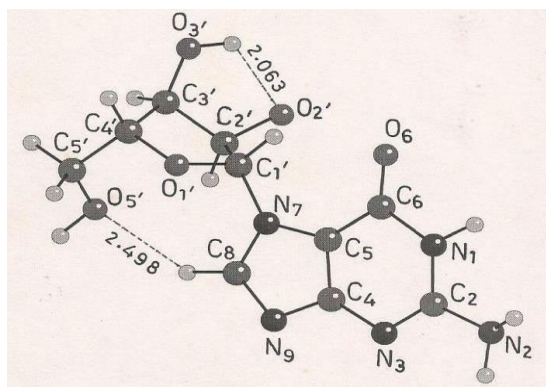
(a) C3'-endo (keto-N9R)



(b) C2'-endo (keto-N9R)

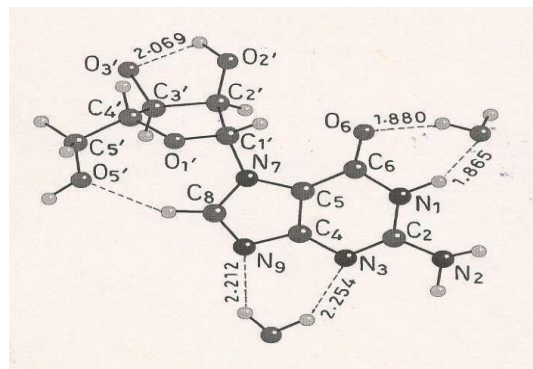


(c) C3'-endo (keto-N7R)

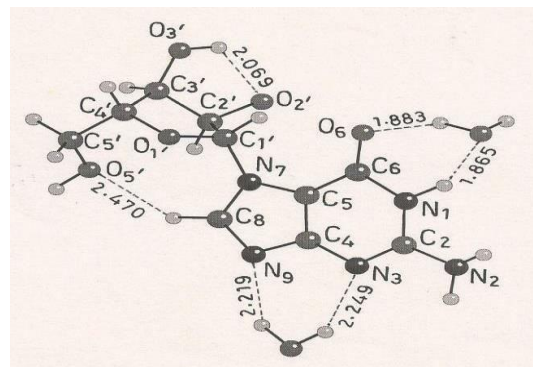


(d) C2'-endo (keto-N7R)

Fig. 1. (a-d) Molecular structures of the anti-conformations of the keto forms of rG

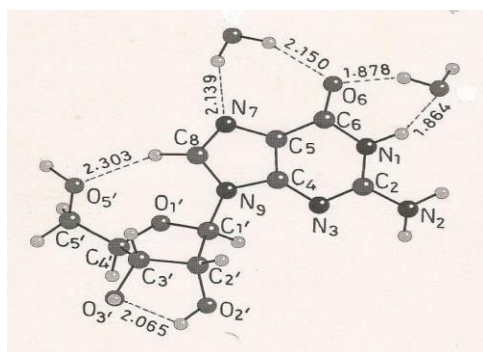


C3'-endo (keto-N7R)-2W

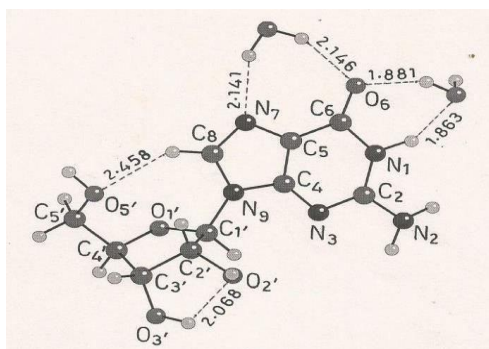


(c) C2'-endo (keto-N7R)-2W

Fig. 2. (a-d) Hydrogen-bonded complexes of the anti-conformations of rG with two water molecules each



(a) C3'-endo (keto-N9R)-2W



(b) C2'-endo (keto-N9R)-2W

III. RESULTS AND DISCUSSION

The relative total energies of the different keto tautomers of the anti-conformations of rG and the corresponding energies of the complexes with two water molecules each in gas phase and aqueous media obtained at the B3LYP/6-31G** levels are presented in Table 1. Further, this table includes the relative total energies of each of the above mentioned systems for C2'-endo and C3'-endo conformations of sugar moiety.

TABLE I. Relative total energies (kcal/mole) of the different keto tautomers of the anti-conformation of rG and its complexes with two water molecules each in gas phase obtained by geometry optimization at the B3LYP/6-31G* level. Each column (B3LYP or MP2) for each conformation has its own reference. R stands for the sugar moiety in rG. In the parenthesis, the values obtained [10] at B3LYP/6-31G* basis set level.

Molecule/Tautomer	B3LYP	MP2
rG		
keto-N9R (R=C3'-endo)	0.0 ^a	0.0 ^a
keto-N9R (R=C2'-endo)	+0.12 (+0.08)	+0.38
keto-N7R (R=C3'-endo)	-0.14	-0.24
keto-N7R (R=C2'-endo)	+0.19	+0.50
rG+2H₂O		
keto-N9R+2H ₂ O (R=C3'-endo)	0.0 ^a	0.0 ^a
keto-N9R+2H ₂ O (R=C2'-endo)	+0.21	+0.58
keto-N7R+2H ₂ O (R=C3'-endo)	-0.08	-0.17
keto-N7R+2H ₂ O (R=C2'-endo)	+1.81	+1.91

^aPresent work

Thus the anti-conformation of keto-N7R form of rG is appreciably more stable than the same conformation of keto-N9R form of the nucleoside in both gas phase and aqueous media at B3LYP and MP2 levels for C3'-endo conformation of the sugar ring.

Hydrogen-bonded complexes of rG with water molecules would be important since they may occur at the water-air interface, and this complexation would correspond to the microscopic solvent effect. For this reason, the geometries of anti-conformations of keto-N9R and keto-N7R forms of rG-2W were optimized in gas phase and subsequently, using these optimized geometries, the species solvated in bulk water. The gas phase geometries of these hydrogen bonded complexes are shown in Fig. 2 where the hydrogen bonding distances are also indicated.

The relative total energies obtained at B3LYP and MP2 levels presented in Table 1 show that the anti-conformations of keto-N7R form of rG and rG-2W with C3'-endo conformation of the sugar rings are more stable in aqueous media than the corresponding forms of the nucleoside where the sugar ring has C2'-endo conformation.

IV. MOLECULAR GEOMETRY

The gas phase optimized structures of anti-conformations of the C3'-endo (keto-N9R), C2'-endo (keto-N9R), C3'-endo (keto-N7R) and C3'-endo (N7R) forms of rG are shown in Figs. 1 (a-d) while the corresponding structures of hydrogen bonded complexes of the anti-conformations of rG with two water molecules each of C3'-endo (keto-N9R), C2'-endo (keto-N9R), C3'-endo (keto-N7R) and C3'-endo (N7R) are shown in Figs. 2 (a-d) respectively. Details of optimized molecular geometries of the keto-N9R and keto-N7R forms of rG for both the C2'-endo and C3'-endo conformations of the sugar ring for the anti-conformation of the nucleoside and hydrogen-bonded complexes of the anti-conformations of rG with two water molecules each of C3'-endo (keto-N9R), C2'-endo (keto-N9R), C3'-endo (keto-N7R) and C3'-endo (N7R) are presented in Tables 2 & 3 respectively. Only some hydrogen-bond parameters data are available [10,11]. Usually the agreement between the gas phase optimized and available data [10,11] was found to be quite good.

TABLE II. The observed and calculated values of some sugar bond lengths (Å), bond angles (deg.) and dihedral angles (deg.) of the different keto tautomers of the anti-conformations of rG each in gas phase obtained by geometry optimization at the B3LYP/6-31G** level. For each bond length, bond angle and dihedral angle, the values are given in two lines, out of which the upper line corresponds to C3'-endo while the lower line corresponds to C2'-endo conformations of the sugar ring in rG.

Geometrical Variables (Bonds/ angles)	Calculated ^a		Observed ^{b,c}
	keto-N9R	keto-N7R	
Bond lengths			
C1' C2'	1.541	1.540	1.529 ^b
O1 C4	1.541	1.541	
	1.433	1.435	
	1.441	1.441	
C2' C3'	1.542	1.542	
	1.540	1.540	

C3' O3'	1.426	1.426	1.417 ^b
	1.415	1.415	
Bond angles			
C1' C2' C3'	102.3	102.0	101.3 ^b
	102.2	102.2	101.5 ^b
O1' C1' C2'	106.7	106.7	107.6 ^b
	106.0	105.9	
C2' C3' C4'	101.8	101.5	
	102.4	102.3	102.6 ^b
C3' C4' C5'	115.2	115.6	
	114.8	114.9	115.2 ^b
Dihedral angles			
C1' O1' C4' C3'	19.0	18.6	15.3 ^c
	-7.1	-6.5	
C1' C2' C3' C4'	33.9	35.4	33.8 ^c
	-33.4	-33.7	
O1' C1' C2' C3'	-24.0	-25.8	-25.0 ^c
	30.4	31.0	

^aPresent work

^bRef. [10]

^cRef. [11]

TABLE III. Intramolecular hydrogen bond parameters^a of the different keto tautomers of the anti-conformations of rG each in gas phase obtained by geometry optimization at the B3LYP/6-31G** level. R stands for the sugar moiety in rG. In the parenthesis, the value obtained at B3LYP/6-31G* basis set level [10].

Molecule/ Tautomer	C-H...O hydrogen bond parameters		
	d(H...O(5'))	d(C...O(5'))	θ(C-H...O(5'))
...			
keto-N9R (R=C(3')-endo)	2.357 (2.356)	3.377(3.375)	156.8 (156)
keto-N9R (R=C(2')-endo)	2.518 (2.542)	3.449 (3.470)	143.7 (143)
keto-N7R (R=C(3')-endo)	2.314	3.320	153.9
keto-N7R (R=C(2')-endo)	2.498	3.436	144.5

^ad(H...O(5')) (Å), d(C...O(5')) (Å) and θ(C-H...O(5')) (deg.) represent hydrogen-acceptor distance, donor-distance and donor-hydrogen-acceptor angle respectively. H and C refer to H(8) and C(8) for rG, respectively.

The present optimized gas phase geometrical parameters of the sugar ring of the anti-conformation of keto-N9R form of rG, including the C2'-endo and C3'-endo conformations of the sugar ring, differ, on the average, from the results reported earlier [10,11] as follows:

- The present bond lengths differ from those obtained earlier by about 0.01Å.
- The present bond angles differ from those obtained at earlier by about 1 deg.
- The present value of the dihedral angles differ from that obtained earlier by about 1.5 deg.
- The present value of the (C8H8...O5') hydrogen bond length differs from those obtained earlier by about 0.025 Å.

The above comparison shows that the B3LYP/6-31G** basis set approach a satisfactory gas phase molecular geometry.

We arrive at this conclusion from this study that the nucleoside rG or its complex rG-2W would occur in both the keto-N9R and keto-N7R forms at the solution-air interface.

This result suggests that mutation may be induced when the nucleoside comes in contact with dissolved oxygen in

biological systems.

Acknowledgment

The authors thank Dr. Arunesh Kumar Yadav and Mr Surender Singh for helpful discussions.

REFERENCES

- [1] M. Chen, W. Lin, L. Hong, N. Ji and H. Zhao "The development and lifetime stability improvement of guanosine-based supramolecular hydrogels through optimized structure," *BioMed Research International*, vol. 2019, pp. 1-18, 2019
- [2] J.D. Watson, A. Gann, T.A. Baker, M. Levine, S.P. Bell, R. Losick "Molecular Biology of Gene," Seventh Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, pp. 107-118, 2013
- [3] M.F. Goodman "Mutation caught in the act," *Nature*, vol. 378, pp. 237-238, 1995
- [4] S.K. Mishra, M.K. Shukla and P.C. Mishra, "Electronic spectra of adenine and 2-aminopurine: an ab initio study of energy level diagrams of different tautomers in gas phase and aqueous solution," *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, vol 56, pp. 1355-1384, 2000
- [5] M.K. Shukla, S.K. Mishra, A. Kumar and P.C. Mishra, "An ab initio study of excited states of guanine in the gas phase and aqueous media: Electronic transitions and mechanism of spectral oscillations," *Journal of Computational Chemistry*, vol. 21, pp. 826-846, 2000
- [6] E. Nir, P. Imhof, K. Kleinermanns and M.S. de Vries, "REMPI spectroscopy of laser desorbed guanosines," *Journal of American Chemical Society*, vol. 22, pp. 8091-8092, 2000
- [7] . Tolosa, J.A. Sansón and A. Hidalgo "Theoretical study of adenine to guanine transition assisted by water and formic acid using steered molecular dynamic simulations," *Frontiers in Chemistry*, vol. 7, pp. 1-11, 2019
- [8] E. Nir, C. Janzen, P. Imhof, K. Kleinermanns and M.S de Vries, "Guanine tautomerism revealed by UV-UV and IR-UV hole burning spectroscopy," *Journal of Chemical Physics*, vol. 115, pp. 4604-4609, 2001
- [9] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.A. Robb, J.R. Cheeseman, T. Keith, G.A. Petersson, J.A. Montgomery, K. Raghavachari, M.A. Al-Laham, V.G. Zakrzewski, J.V. Ortiz, J.B. Foresman, J. Cioslowski, B.B. Stefanov, A. Nanayakkara, M. Challacombe, C.Y. Peng, P.Y. Ayala, W. Chen, M.W. Wong, J.L. Andres, E.S. Replogle, R. Gomperts, R.L. Martin, D.J. Fox, J.S. Binkley, D.J. Defrees, J. Baker, J.P. Stewart, M. Head-Gordon, C. Gonzalez and J.A. Pople, *Gaussian 94, Revision E.3*, Gaussian, Inc., Pittsburgh PA (1995)
- [10] A. Hocquet, N. Leulliot and M. Ghomi, "Ground-State Properties of Nucleic Acid Constituents Studied by Density Functional Calculations. 3. Role of Sugar Puckering and Base Orientation on the Energetics and Geometry of 2'- Deoxyribonucleosides and Ribonucleosides," *Journal of Physical Chemistry B*, vol. 104, pp. 4560-4568, 2000
- [11] C. Altona and M. Sundaralingam, "Conformational analysis of the sugar ring in nucleosides and nucleotides. New description using the concept of pseudorotation," *Journal of American Chemical Society*, vol. 94, pp. 8205-8212, 1972

