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DFT STUDY OF Cu^+ AND Zn^{2+}- URACIL COMPLEXES IN THE GAS PHASE : HOMO-LUMO APPROACH

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ABSTRACT

DFT study of the interaction of uracil, a RNA base, with Zn^{2+} and Cu^+ ion is carried out. Most favorable sites of attachment of these ions in uracil are determined with the help of metal ion affinity (MIA) values. The two oxygen atoms of uracil are found to be the most susceptible sites of attachments of metal ions. Mulliken population analysis (MPA) method is used to determine the Mulliken charges of basic sites as well as the metal ions in all complexes. Possible correlation between the MIA and the retained charges of metal ions is thoroughly explored. Energies of frontier orbitals (HOMO and LUMO) also correlate with the MIA values.

Key words: Uracil, DFT, HOMO, LUMO, Zn^{2+}, Cu^+ ions.

INTRODUCTION

Metal ions play vital role in numerous biological processes; especially their roles in the structural stabilization and functioning of nucleic acids, proteins, enzymes, peptide hormones are being widely reported in many studies[1]. Zn and Cu are two essential trace elements, required for normal metabolic processes. Both the metals combine with many proteins to produce biologically significant enzymes[2]. Zinc is present in all body fluids and tissues. It is an essential component of a large number of enzymes, which participate in various processes like synthesis and degradation of carbohydrates, proteins, nucleic acids and in the metabolism of other micronutrients[3]. It takes roles in the metabolism of RNA and DNA, signal transduction, as well as in the gene expression. Carbonic anhydrase and carboxy peptidase are two important enzymes of Zn, which have their roles in the processes of CO_2 regulation and in the cleavage of peptide linkages during the digestion of proteins respectively. Zinc fingers help in the analysis of DNA sequences. Zn^{2+} ions in zinc fingers help in maintaining its structure by binding to four amino acids in the transcription factor,

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which in turn binds the DNA helix and thus helps in communicating with other cells[4]. Similarly, metalloenzymes which contain Cu^+ ion in their active centre are most frequently used for the catalysis of the oxidation- reduction processes. Both of Zn and Cu are absorbed in the metallothionein reserves and hence inadequate or excessive zinc intake can be harmful; excess zinc particularly impairs the copper absorption[2,5].

Recently, Zhu and his co workers studied on the interaction of NH_4^+ with many heterocyclic compounds, which paved out the way for the study of cationic ions and π-systems in proteins and nucleic acids in the gas phase using the DFT method[6,7]. Such studies enable researchers to determine the structure as well as many thermodynamic parameters of the metal ion-organic molecule complexes, most favorable site of attachment of the metal ion in the target molecule, comparative metal ion affinities of different sites etc. Proper understanding of such complexes helps in the designing of new catalysts, drugs, enzymes etc[8]. In many instances direct experimental studies of the interaction of metal ions with nucleic acids has been found to be highly tedious and time consuming task. However, theoretical studies using sufficient basis sets and intrinsic binding models can help experimental researchers in accumulating information regarding their structures, interaction energies, thermodynamics etc and thus help in eliminating guess works to many extents[9-11].

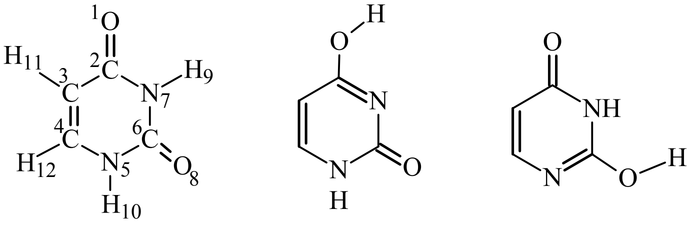
EXPERIMENTAL

Computational method

Uracil is one of the four nucleobases of RNA and it binds with adenine via two H-bonds. There are four basic sites in the molecule, in which Zn (II) and Cu (I) ions can attach. The most favorable attachment will involve the lowest energy and the same is determined with the help of metal ion affinities (MIA) values, which are assumed to the negative of the enthalpy change during the following complexation process, M^{n+} ion (Zn^{2+} or Cu^+ ion) + Uracil → M^{n+}-Uracil complex Alternatively, MIA or $-\Delta H = [E^0 (M^{n+}) + E^0$ (Uracil)] - E^0 (M^{n+}- Uracil complex)] Where, E^0 represents absolute energies of species. All optimization and frequency calculations are done using B3LYP[12] with 6-31G** basis sets as incorporated in the Gaussian 09' programme code (G09W)[13] in the gas phase. The basis set 6-31G (d, p) is large enough to reduce the basis set superposition error (BSSE)[14] to ~2-3 Kcal/mol[15]. Hence, in the present work, correction due to BSSE was not taken into account. HOMO-LUMO energies of all the metal ion-uracil complexes are determined using the Gaussian programme and the same basis sets as above. Free energy changes (ΔG^0) during complexations at various positions are calculated at 298.15 K and 1 atmosphere pressure in the gas phase using the same basis sets. ΔG^0 is assumed to be the difference between the total free energies of the products and reactants. In all the calculations due consideration is given to the thermal corrections to the Gibbs free energy.

RESULTS AND DISCUSSION

At first all the stable tautomers of uracil are determined using G09W software (Fig. 1). U1 has been found to be the most stable tautomer with absolute energy of – 414.8258 hartee, while U2 and U3 are less stable than U1 with energies of – 414.8065 hartee and – 414.7948 hartee, respectively. Obviously U1 is energetically most stable and hence all complexations are studied with U1. Zn^{2+} and Cu^{+} ions are placed at different basic sites around it (viz. O1, N7, O8 and N5 of U1, Fig. 1) and metal complexes so obtained are fully optimized with the B3LYP/6-31G** method using Gaussian software. All the optimized geometries of the metal ion-uracil complexes are shown in Fig. 2-6. All the complexes are mono co-ordinated and metal ions are seen to interact with the oxygen atoms only. Metalation of uracil results two types of complexes, viz. O1 and O8 complexes. Metalation at N5 and N7 of uracil produces unstable complexes and ultimately metal ions migrate to either of the two oxygen atoms for producing geometries those are energetically more favorable (Fig. 3, 6).



U1 **U2** **U3**

Fig. 1: Stable tautomers of Uracil as obtained by G09W software

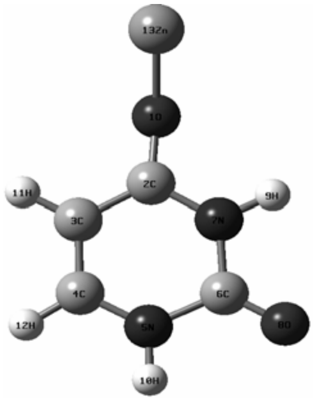


Fig. 2: Zn^{2+}-U1 (O1) Complex (N5) Complex

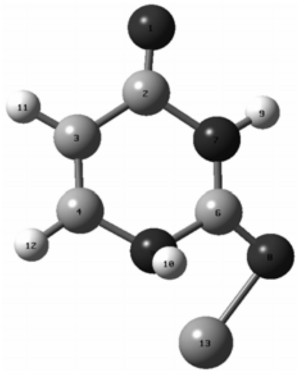


Fig. 3: Zn^{2+}-U1 (N5) Complex

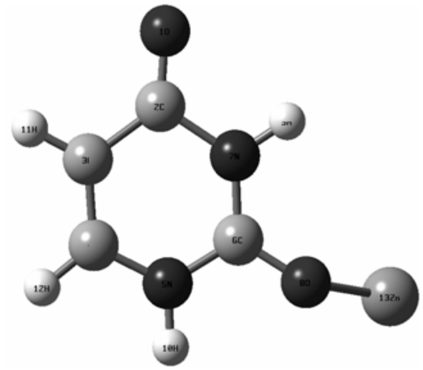


Fig. 4: Zn^{2+}-U1 (O8) Complex

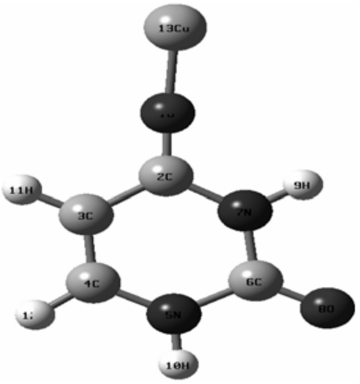


Fig. 5: Zn^{2+}-U1 (O1) Complex

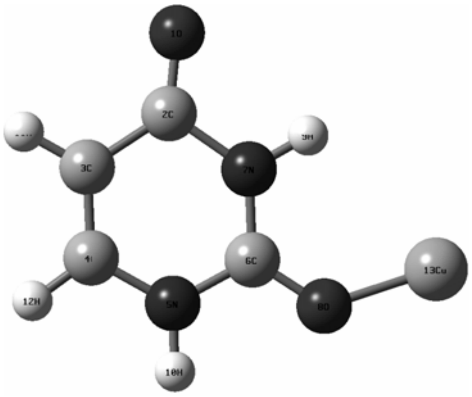


Fig. 6: Optimized structure of Cu$^+$-U1 (O8), Cu$^+$-U1 (N5) Cu$^+$-U1 (N7) Complexes [In all these cases, Cu$^+$ ion is attached to O8 position after optimization]

Computed metal ion affinities (MIA's) for metalation at different sites along with the corresponding ΔG^0 values are given in the Table 1. In either case, metalation at O1 possesses the highest MIA as well as the lowest ΔG^0. Hence, metalation at O1 produces the most stable M^{n+} (Zn^{2+} or Cu$^+$) -Uracil complexes. Mulliken net charges of metal ions as well as the basic sites of the optimized geometries are given in Table 2. To see the possible correlation between the retained charges of metal ions and MIA values, the two parameters are plotted (Fig. 7 and 8). In the case of Zn^{2+}-uracil complexes, MIA values vary inversely with the retained charge of the metal ion. On the other hand, In the case of Cu$^+$-Uracil complexes, MIA values vary directly with the retained charge of the metal ion. Table 2 shows that at an average of 0.72 and 0.31 units of negative charges are transferred from the uracil base to the Zn and Cu-atoms respectively.

Table 1: Computed metal ion affinities (MIA's) (B3LYP/6-31G) of M^{n+}-Uracil (U1) complexes and standard free energy (ΔG^0) changes during their formation.**

S. No.	Complexes	Zn^{2+}-Uracil complex		Cu^{+}-Uracil complex	
		Standard free energy change with the correction due to internal energy (ΔG^0)	MIA (Kcal/mol)	Standard free energy change with the correction due to internal energy (ΔG^0)	MIA (Kcal/mol)
1	**M^{n+}-U1(O1)**	-175.5387	183.4702	--85.3270	93.9432
2	**M^{n+}-U1(O8)**	-165.5216	173.0509	-82.6061	90.7411
3	**M^{n+}-U1(N5)**	-154.6272	162.5609	-82.6011	90.7411
4	**M^{n+}-U1(N7)**	-174.3935	174.5214	-82.6023	90.7411

Table 2: Computed Mulliken Net charges (Q/e) on various atoms of metal ion-uracil complexes

Complex	Positions	Mulliken charge (Q/e)	Complex	Positions	Mulliken charge (Q/e)
Zn^{2+}-U1 (O1)	O1	-0.6577	**Zn^{2+}-U1 (N5)**	O1	-0.2858
	N5	-0.5154		N5	-0.7320
	N7	-0.5895		N7	-0.5449
	O8	-0.3338		O8	-0.5214
	Zn	1.2945		Zn	1.3080
Zn^{2+}-U1(O8)	O1	-0.3311	**Zn^{2+}-U1(N7)**	O1	-0.1736
	N5	-0.5166		N5	-0.5348
	N7	-0.5833		N7	-0.7349
	O8	-0.6461		O8	-0.5293
	Zn	1.2695		Zn	1.2803
Cu^{+}-U1(O1)	O1	-0.6188	**Cu^{+}-U1(N5)**	O1	-0.4243
	N5	-0.5546		N5	-0.5576
	N7	-0.5992		N7	-0.5971
	O8	-0.4248		O8	-0.5881
	Cu	0.7035		Cu	0.6784

Cont…

Complex	Positions	Mulliken charge (Q/e)	Complex	Positions	Mulliken charge (Q/e)
Cu$^+$-U1(O8)	O1	-0.4243	**Cu$^+$-U1(N7)**	O1	-0.4244
	N5	-0.5575		N5	-0.5575
	N7	-0.5971		N7	-0.5971
	O8	-0.5882		O8	-0.5881
	Cu	0.6783		Cu	0.6783

Table 3: Computed HOMO-LUMO energies in metal ion-uracil complexes

Complex	HOMO-LUMO energies (a.u.) (B3LYP/6-31G**)		Difference (in Kcal/mol)	MIA (Kcal/mol)
Zn^{2+}-U1 (O1)	HOMO	-0.5756	26.0107	183.4702
	LUMO	-0.5341		
Zn^{2+}-U1 (N5)	HOMO	-0.6144	49.3858	162.5609
	LUMO	-0.5357		
Zn^{2+}-U1 (N7)	HOMO	-0.6109	82.9707	174.5214
	LUMO	-0.4787		
Zn^{2+}-U1 (O8)	HOMO	-0.5753	22.4338	173.0509
	LUMO	-0.5395		
Cu$^+$- U1 (O1)	HOMO	-0.3904	82.2114	93.9432
	LUMO	-0.2594		
Cu$^+$- U1 (N5)	HOMO	-0.4040	85.0541	90.7411
	LUMO	-0.2685		
Cu$^+$- U1 (N7)	HOMO	-0.4040	85.0541	90.7411
	LUMO	-0.2685		
Cu$^+$- U1 (O8)	HOMO	-0.4039	85.0603	90.7411
	LUMO	-0.2684		

Table 4: Selected bond lengths (in Å) in the most stable metal ion-uracil complexes obtained by B3LYP/6-31G calculation**

Zn^{2+}- Uracil (O1)		Uracil	Cu^{+}- Uracil (O1)	
Bond	**Bond Length (Å)**	**Bond Length (Å)**	**Bond**	**Bond Length (Å)**
Zn-1O	1.7903	-	Cu-1O	3.9715
1O = 2C	1.3155	1.2194	1O = 2C	1.2624
2C-7N	1.3533	1.4126	2C-7N	1.3698
7N-6C	1.4190	1.3847	7N-6C	1.4069
6C = 8O	1.1925	1.2166	6C = 8O	1.2042
6C-5N	2.3522	1.3948	6C-5N	1.3984

*Positions of atoms in metal ion-uracil complexes are shown in Fig.1, U1

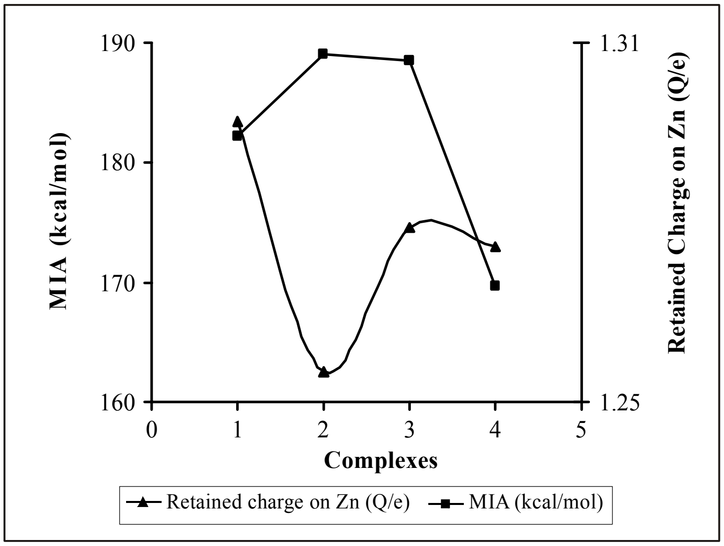


Fig. 7: Correlation between the MIA (in Kcal/mol) and retained charge (Q/e) of Zn

B3LYP/6-31G** studies of the two metal ions show that the LUMO energies of Zn^{2+} and Cu^{+} ions are – 0.7838 a.u. and – 0.3499 a.u. respectively. Clearly, Zn^{2+} has the lower LUMO energy, which accounts for the higher charge transfer in Zn^{2+}-uracil complexes than that in Cu^{+}-uracil complexes. The higher charge transfer in turn accounts for the higher MIA values of Zn^{2+}-uracil complexes than that of Cu^{+}-uracil complexes. Computed Energies of frontier orbitals in the optimized geometries as obtained by Gaussian calculations are shown in the Table 4. In the case of Cu^+-uracil complexes, those with higher HOMO-LUMO energy gaps possessed lower MIA values. The correlation is confirmed by plotting HOMO-LUMO energy differences and MIA values of all the complexes (Fig. 9 and 10). However, in the case of Zn^{2+}-uracil complex similar correlation is not seen. Rather, in some instances MIA values are seen to rise with the lowering of the HOMO-LUMO energy gaps. Bond lengths of a few selected bonds are shown in the Table 4. The elongation of the 2C = 1O bond length (usual C = O bond length is 1.20Å) after metalation in either cases, indicates the possible charge transfer from oxygen (i.e. 1O) to the metal atom.

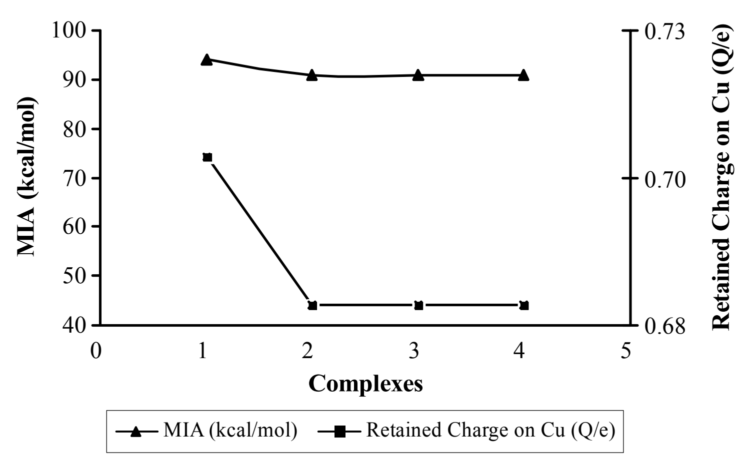


Fig. 8: Correlation between the MIA (in Kcal/mol) and retained charge (Q/e) of Cu

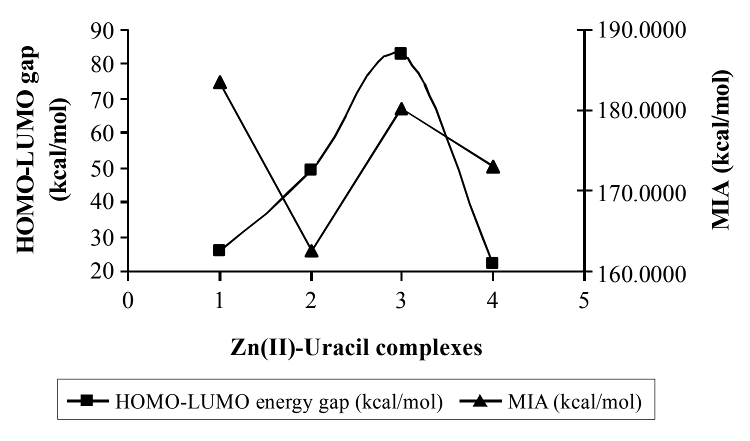


Fig. 9: Correlation between the MIA and the difference between the HOMO-LUMO energies of Zn^{2+}-Uracil complexes

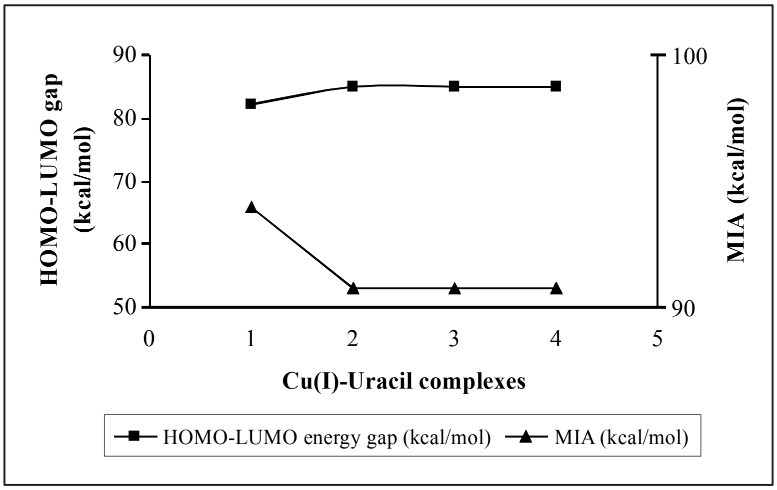


Fig. 10: Correlation between the MIA and the difference between the HOMO-LUMO energies of Cu^+-Uracil complexes

CONCLUSION

(i) Zn^{2+} or Cu^+ ion may undergo complexation either at O1 or at O8 position of uracil but the most stable complex results by the interaction at the O1 position. It is evident from their ΔG and MIA values.

(ii) Zn^{2+}-uracil complexes have higher metal ion affinities than Cu^+-uracil complexes. Both the complexes show similar trends in the variation of MIA values.

(iii) The change of MIA can be correlated to the retained charges of metal atoms. There exists contrasting correlations in the two cases. Cu^+-uracil complexes exhibit increase in MIA values with the increase in the retained charge on Cu. On the other hand, in the case of Zn^{2+}-uracil complexes, MIA values decrease with increase in the retained charge on the metal atom, the variation is not predictably regular.

(iv) Charge transfer is more in the case of Zn^{2+}-uracil complexes than that in the case of Cu^+-uracil complexes, which accounts for the higher MIA values of Zn^{2+}-complexes.

(v) Variation of MIA with the HOMO-LUMO energy gap is not regular in the case of Zn^{2+}-uracil complexes but in the case of Cu^+-uracil complexes, MIA values are seen to decrease with increasing HOMO-LUMO energy gap.

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REFERENCES

1. S. Lippard and J. M. Berg, Principles of Bioinorganic Chemistry, University Science Books, Mill Balley, CA (1994).
2. J. H. Weil, General Biochemistry, New Age Int. Ltd. Publishers, France (1996).
3. A. Siegel and H. Siegel, Metal Ions in Biological Systems, **32**, Marcel Decker Inc., New York (1996).
4. J. P. Mackay and M. Crossley, Trends Biochem. Sci., **23**, 1 (1998).
5. F. Briganti, S. Mangani, P. Orioli, A. Scozzafava, G. Vernaglione and C. T. Supuran, Biochemistry, **36**, 10384 (1997).
6. W. L. Zhu, H. L. Jiang, C. M. Puah, X. J. Tan, K. X. Chen, Y. Cao and R. Y. Ji, J. Chem. Soc., Perkin Trans., **2**, 2615 (1999).
7. R. G. Parr and W. Yang, Density Functional Theory of Atoms and Molecules, Oxford University Press, Oxford, UK (1989).
8. Y. J. Zhang and K. M. Merz, J. Comput. Chem., **13(9)**, 1151 (1992).
9. N. Russo, T. Marino, M. Toscano and A. Grand, J. Quant. Chem., **98**, 347 (2004).
10. N. Russo, M. Toscano and A. Grand, J. Mass Spect., **38**, 265 (2003).
11. N. Russo, M. Toscano and A. Grand, J. Am. Chem. Soc., **123**, 10272 (2001).
12. A. D. Becke, J. Chem. Phys., **98**, 5648 (1993).
13. M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman et al., Gaussian, **94**, Gaussian Inc., Pittsburgh PA (1995).
14. S. F. Boys and F. Bernardi, Mol. Phys., **19**, 553 (1970).
15. L. Rulı´sˇek and Z. Havlas, J. Am. Chem. Soc., **122**, 10428 (2000).

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