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Research Article

DFT STUDY OF Co^{2+} AND Fe^{2+}- URACIL COMPLEXES IN THE GAS PHASE

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ABSTRACT

Metal ion affinities of Fe^{2+}-Uracil and Co^{2+}-Uracil complexes are determeined using DFT method and 6-31G** basis set. O1 and N7 atoms of Uracil are the most susceptible sites of attachments of Fe^{2+} and Co^{2+} ions respectively. Complexes are either bi coordinated or mono coordinated. The site at which the metal ion attachment occurs, witnesses a net accumulation of negative charge density which in turn accounts for the stability of the complex. A fair correlation exits between the retained charges on metal ions and charge transfer in complexes. Co^{2+} complex at N7 of Uracil possesses the highest HOMO-LUMO energy gap as well as the highest MIA. However, similar correlation is not seen in the case of Fe^{2+}-Uracil complexes.

Keywords: Uracil, MIA, Mulliken atomic charges, HOMO-LUMO, retained charges on metal ions.

INTRODUCTION

Nucleic acids are negatively charged polynucleotides, the negative charge of each nucleotide unit is being carried by the phosphate moiety. The negative ions are counterbalanced by cations lying on their surface. Although nucleic acids contain large number of possible sites for the attachment of metal ion, the phosphate group constitutes the primary binding site. Attachment of metal ions with the phosphate groups along the sugar-phosphate backbone helps in reducing and hence neutralizing electrostatic repulsions between adjacent anionic phosphate moieties of nucleic acid polymers. Direct attachment of metal ions with phosphate groups is mostly hindered by the presence of a jacket of polar solvent. Sometimes, metal cations attached to phosphate group may catalyse the hydrolysis of the phosphodiester linkage in RNA[1-2]. Studies of sponer *et al* showed that although the gas phase interactions are dominated by the electrostatic interaction, but in the polar solvent it is eliminated. Rather gas phase data can be transformed into solution with the help of continuum solvent techniques or by using the charge dependence of the gas phase results[3]. Other possible interactions being metal-nucleobase interactions, metal-base pair interaction, metal-nucleotide interactions under different physiological conditions. The binding energy of the metal-nucleic acid complex depends on the site at which the metal ion gets attached[4-6].

Recently, Russo and his co workers carried out several studies on the interaction of metal ions with RNA, DNA bases and it is seen that computational methods can provide useful information about different metal ion-nucleobase complexations. Thus, theoretical studies may help experimental chemists by providing them information regarding structures, interaction energies, thermodynamics etc and thus help in eliminating guess works to many extents[4-9].

In our past studies carried out on the interaction of few metal ions with nucleobases using DFT methods[10] emerged some important correlations between the energies of frontier orbitals of metal ions, charges retained on metal ions involved in complexations as well as the HOMO-LUMO energy gap in the optimized complexes with the metal ion affinities and hence stabilities of metal ion-nucleobase complex[11-12]. In the present case, we aim to investigate the afforsaid correlation in Co^{2+} and Fe^{2+}-Uracil complexes using DFT method with 6-31G** basis sets.

COMPUTATIONAL METHOD

Uracil is one of the four nucleobases of RNA with four nucleophillic sites in the molecule in which the two metal ions can attach. The most favourable site of attachment is studied with the help of metal ion affinity (MIA) values. All the geometries are optimized using the Gaussian programme code[13]. MIA values are assumed to be the negative value of the enthalpy change occurring in the following complexation processs.

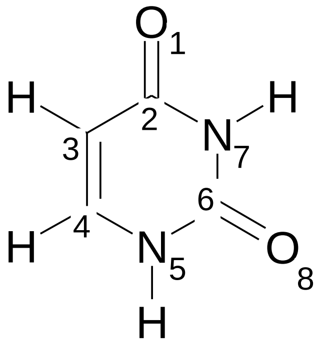
Co^{2+} + Uracil$\rightarrow$ Co^{2+}-Uracil complex

Fe^{2+} + Uracil$\rightarrow$ Fe^{2+}-Uracil complex

Higher the stability of the complex, higher is the enthalpy evolved and hence higher will be the positive value of MIA which is determined mathematically as

MIA = $[E^0 (Co^{2+}$ or $Fe^{2+}) + E^0$ (Uracil)] – $[E^0 (Co^{2+}$ or Fe^{2+}- Uracil complex)]

Where, E^0 represents absolute energies of respective species. In all optimizations and frequency calculations are done using B3LYP[14] with 6-31G (d, p) basis sets as incorporated in the Gaussian programme in the gas phase. HOMO LUMO energies (in kcal/mol) are extracted from the optimized geometries. The corresponding energy gaps between the two are also determined and tried to correlate with the observed trend of variation of MIA values.



U1

Fig. 1: Stable tautomer of uracil as obtained by G09W software

RESULTS AND DISCUSSIONS

Earlier studies[6, 14] on Uracil suggest that U1 as shown in the figure 1 is the most stable tautomer of Uracil. All the complexetions of Uracil with Co^{2+} or Fe^{2+} are studied with the above tautomer. U1 and all metal ion-uracil complexes are fully optimized with Gaussian programme using B3LYP/6-31G** method. Optimised geometries of Co^{2+}/ Fe^{2+}-Uracil complexes at all possible co ordination sites are given in figures 2-9. In all complexes metal atoms are seen to be attached to O-atoms only, after optimization. All the complexes are either mono co-ordinated or bi coordinated and the metalation takes place either at O1 or at O8 of uracil.

In table 1, metal ion affinities (MIA's) as calculated by the DFT method are reported. It shows that the most favourable sites of attachments of Co^{2+} or Fe^{2+} with uracil are different. Fe^{2+} is preferably attached to O1, while Co^{2+} is attached to N7 of uracil. MIA value of Fe^{2+}-Uracil(O1) complex is higher than that of Co^{2+}-Uracil(N7). Table 2, shows the retained charges of various atoms in the metal-uracil complexes. It is interesting to observe that the atom at which metallation occurs possesses the highest negative charge in respective complexes. E.g. in Fe^{2+}-U1(N5) complex, in which Fe^{2+} is attached to N5 of uracil, N5 has the highest accumulation of negative charge (-0.7233 units, table2) as compared to the other nucleophillic sites of the same complex. Similarly, in complexes like Fe^{2+}-U1(N7), Fe^{2+}-U1(O1) etc., highest negative charge accumulation is seen in respective sites of attachments i.e. N7 and O1 respectively. DFT studies of uracil with the same basis set (6-31G**) shows that before complexation, O1, N5, N7 and O8 atoms possess atomic charges of -0.4972, -0.5655, -0.6090 and -0.4941 units respectively. Comparing these values with the atomic charges of respective atoms of Fe^{2+}-U1(N5) complex show that negative charges of O8 and N5 increases after complexation, while those of O1, N7 decrease after the attachment of metal ion. This is an indication of bi coordination of Fe^{2+} ion in this complex. The optimized geometry of the complex (figure 2) shows that Fe^{2+} lies midway between O8 and N5, unlike O1 and O8 complexes, in which mono coordination is evident infigures 4 and 5. Comparision of mulliken net charges of basic sites of Fe^{2+}-Uracil(O1) and Fe^{2+}-Uracil(O8) complexes before and after complexation, shows a net increase of charges of O1 and O8 respectively in these two complexes. Negative charges of other nucleophillic centers decrease after metallation. Similarly, bi coordination is seen in the case of Fe^{2+}-U1 (N7) complex. Comparision of Mulliken net charges of basic sites of Co^{2+}-U1 complexes with corresponding values of uracil indicates bi coordination in Co^{2+}-U1(N5) and Co^{2+}-U1(N7) complexes, while mono coordination is seen in the cases of Co^{2+}-U1(O1) and Co^{2+}-U1(O8) complexes. Corresponding optimized geometries of Co^{2+}-Uracil complexes are shown in figures 6-9.

The variation of MIA's with the retained charges of metal atoms are shown in figures 10 and 11. In table 3, values of energies of frontier orbitals (HOMO and LUMO) and their differences are recorded. To study the possible correlation between the HOMO-LUMO gap and the MIA's, two graphical plots are given in figures 12 and 13. In table 4, bonding parameters in the most stable metal ion-Uracil complexes are given. At the same time corresponding bond lengths are compared with those of Uracil. The elongation of O1-C2 bond in Fe^{2+}-U1 (O1) complex is due to the charge transfers taking place in this complex from O atom to the Fe^{2+} ion. Similar elongation is seen in the case of C6=O8 bond in Co^{2+}-U1(N7) complex, which is an indication of bi coordination of Co^{2+} ion in this complex. The elongation of C2-N7 bond also results due to the attachment of Co^{2+} ion at N7 position. DFT calculation of Co^{2+} and Fe^{2+} ions show that LUMO energies of the two ions are -456.56 and -442.76kcal/mol respectively. The lower value of the LUMO energy of Co^{2+} ion suggests that charge transfer in Co^{2+} -uracil complex is easier than that in Fe^{2+}-uracil complex. It accounts for the lower values of retained charges on Co-atoms in Co^{2+}-uracil complexes as compared to those in Fe^{2+}-uracil complexes.

Table 1: Computed metal ion affinities (MIA's) (B3LYP/6-31G) of M^{2+}-Uracil (U1) complexes**

Sl. No	Complexes	Fe^{2+}-Uracil complex MIA (kcal/mol)	Co^{2+}-Uracil complex MIA (kcal/mol)
1	**M^{n+}-U1 (N5)**	139.7291	159.2884
2	**M^{n+}-U1 (N7)**	145.0146	165.7167
3	**M^{n+}-U1(O1)**	167.9522	161.1637
4	**M^{n+}-U1(O8)**	155.1168	149.5997

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)
Fe^{2+}-U1 (N5)	O1	-0.2995	**Co^{2+}-U1 (N5)**	O1	-0.2894
	N5	-0.7233		N5	-0.7416
	N7	-0.5447		N7	-0.5446
	O8	-0.5736		O8	-0.5328
	Fe	1.3979		Co	1.3257
Fe^{2+}-U1 (N7)	O1	-0.2826	**Co^{2+}-U1 (N7)**	O1	-0.2591
	N5	-0.5115		N5	-0.5137
	N7	-0.8159		N7	-0.8147
	O8	-0.5481		O8	-0.5169
	Fe	1.3875		Co	1.3200
Fe^{2+}-U1 (O1)	O1	-0.7245	**Co^{2+}-U1 (O1)**	O1	-0.6894
	N5	-0.5317		N5	-0.5227
	N7	-0.5935		N7	-0.5931
	O8	-0.3519		O8	-0.3403
	Fe	1.4594		Co	1.3543
Fe^{2+}-U1 (O8)	O1	-0.3542	**Co^{2+}-U1 (O8)**	O1	-0.3347
	N5	-0.5378		N5	-0.5233
	N7	-0.5845		N7	-0.5846
	O8	-0.7184		O8	-0.6712
	Fe	1.4709		Co	1.2863

Table 3: Computed HOMO-LUMO energies in M2+-Uracil complexes

Complex	HOMO-LUMO energies (a.u.) (B3LYP/6-31G**)		Difference (kcal/mol)	MIA (kcal/mol)
Fe^{2+}-U1 (N5)	HOMO	-0.6018	68.5661	139.7291
	LUMO	-0.4925		
Fe^{2+}-U1 (N7)	HOMO	-0.6019	79.2368	145.0146
	LUMO	-0.4756		
Fe^{2+}-U1 (O1)	HOMO	-0.5563	45.4556	167.9522
	LUMO	-0.4838		
Fe^{2+}-U1 (O8)	HOMO	-0.5519	35.9015	155.1168
	LUMO	-0.4947		
Co^{2+}- U1 (N5)	HOMO	-0.6118	73.1894	159.2884
	LUMO	-0.4952		
Co^{2+}- U1 (N7)	HOMO	-0.6085	82.6306	165.7167
	LUMO	-0.4768		
Co^{2+}- U1 (O1)	HOMO	-0.5720	59.8401	161.1637
	LUMO	-0.4767		
Co^{2+}- U1 (O8)	HOMO	-0.5785	68.5473	149.5997
	LUMO	-0.4692		

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

Fe^{2+}- Uracil(O1)		Uracil	Co^{2+}- Uracil(N7)	
Bond	**Bond Length (Å)**	**Bond Length (Å)**	**Bond**	**Bond Length (Å)**
Fe-1O	1.7545	-	Co-1O	3.8349
1O=2C	1.3227	1.2194	1O=2C	1.1721
2C-7N	1.3492	1.4126	2C-7N	1.6957
7N-6C	1.4232	1.3847	7N-6C	1.4316
6C=8O	1.1928	1.2166	6C=8O	1.2739
6C-5N	1.4138	1.3948	6C-5N	1.3196

[* Positions of atoms in M^{2+}-Uracil complexes are shown in Figure 1, U1]

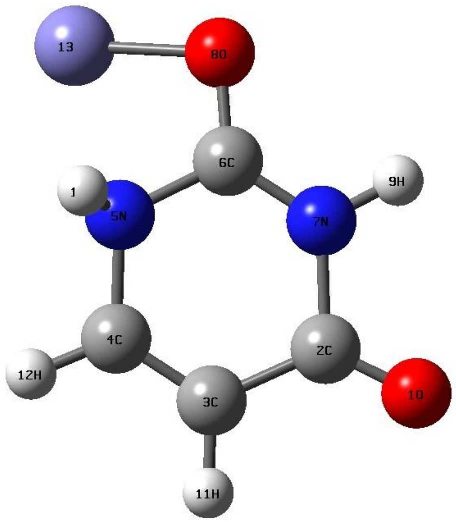


Fig. 2: Fe^{2+}-U1 (N5) Complex

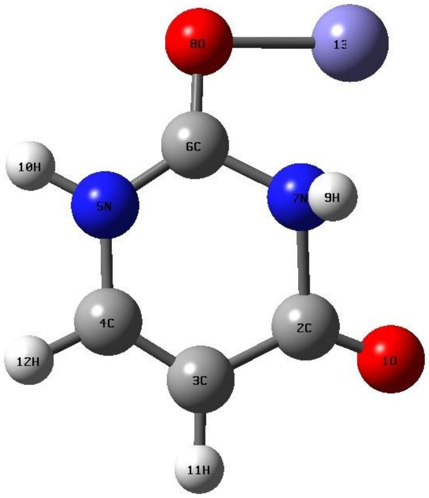


Fig. 3: Fe^{2+}-U1 (N7) Complex

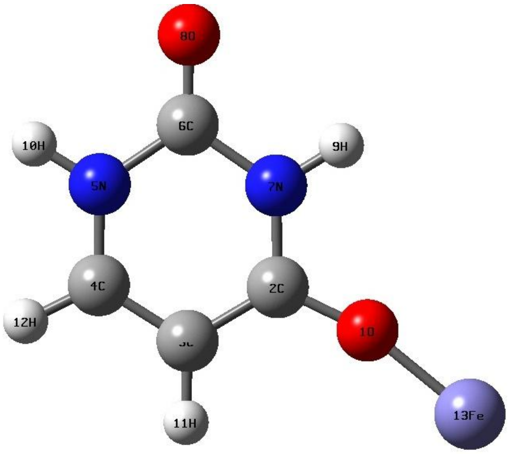


Fig. 4: Fe^{2+}-U1 (O1) Complex

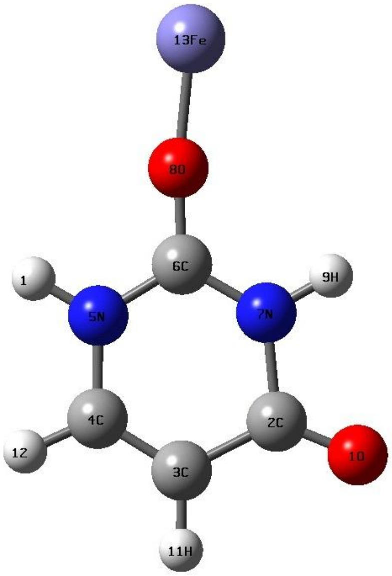


Fig. 5: Fe^{2+}-U1 (O8) Complex

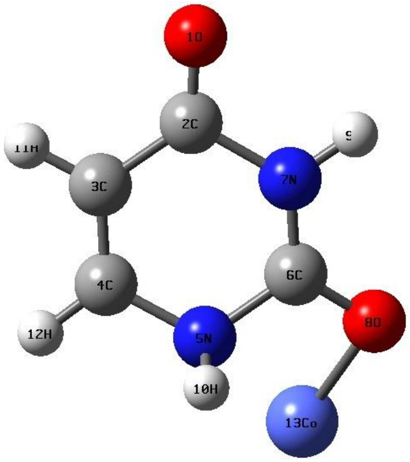


Fig. 6: Co^{2+}-U1 (N5) Complex

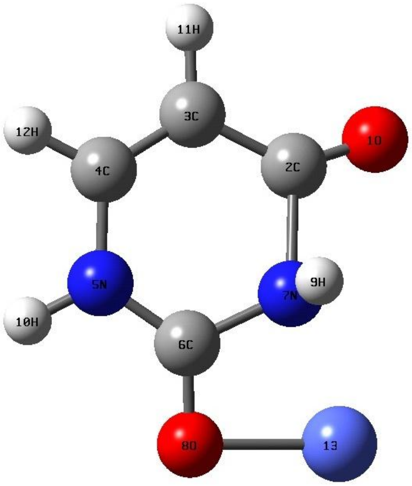


Fig. 7: Co^{2+}-U1 (N7) Complex

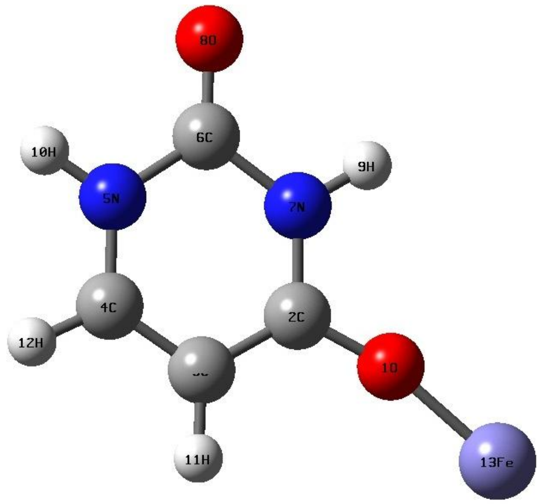


Fig. 8: Co^{2+}-U1 (O1) Complex

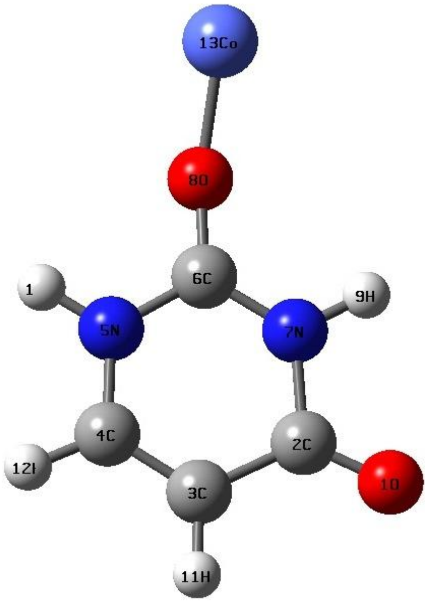


Fig. 9: Co^{2+}-U1 (O8) Complex

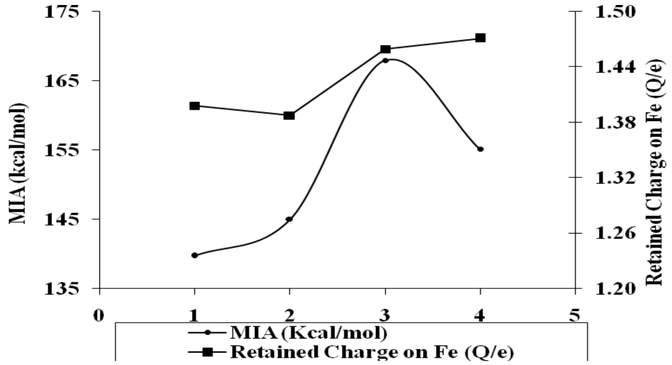


Fig. 10: Correlation between the MIA (in kcal/mol) and retained charge (Q/e) of Fe

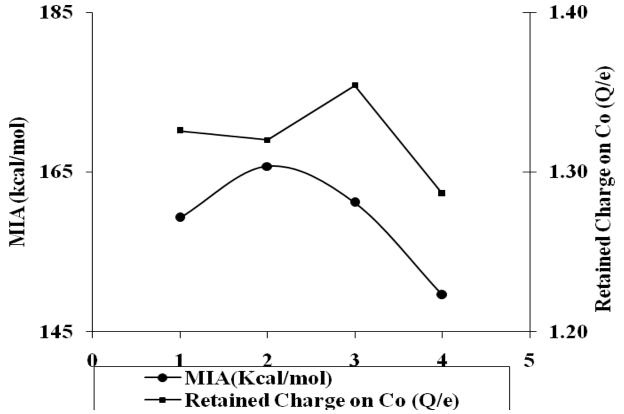


Fig. 11: Correlation between the MIA (in kcal/mol) and retained charge (Q/e) of Co

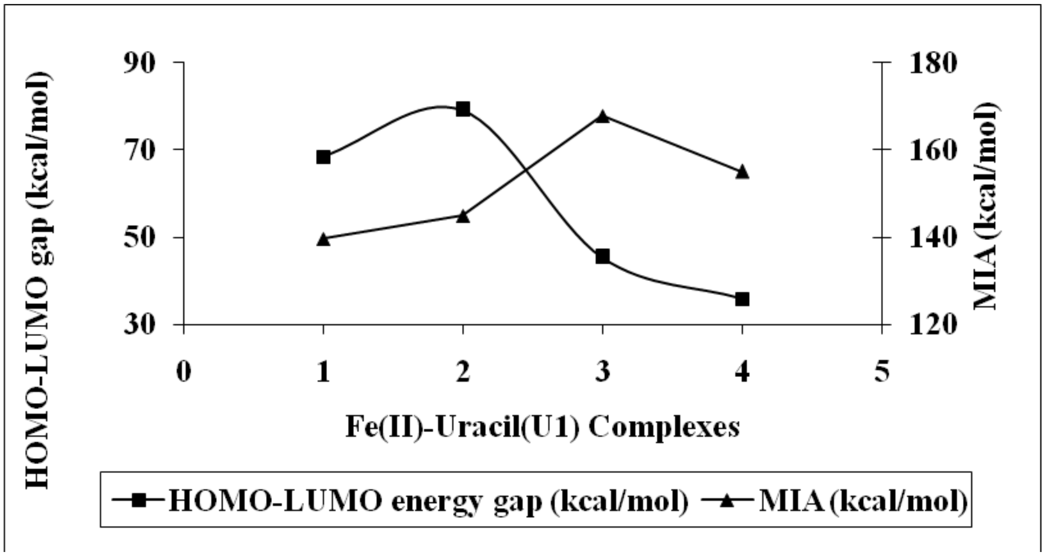


Fig. 12: Correlation between the MIA and the difference between the HOMO-LUMO energies of Fe^{2+}-Uracil complexes

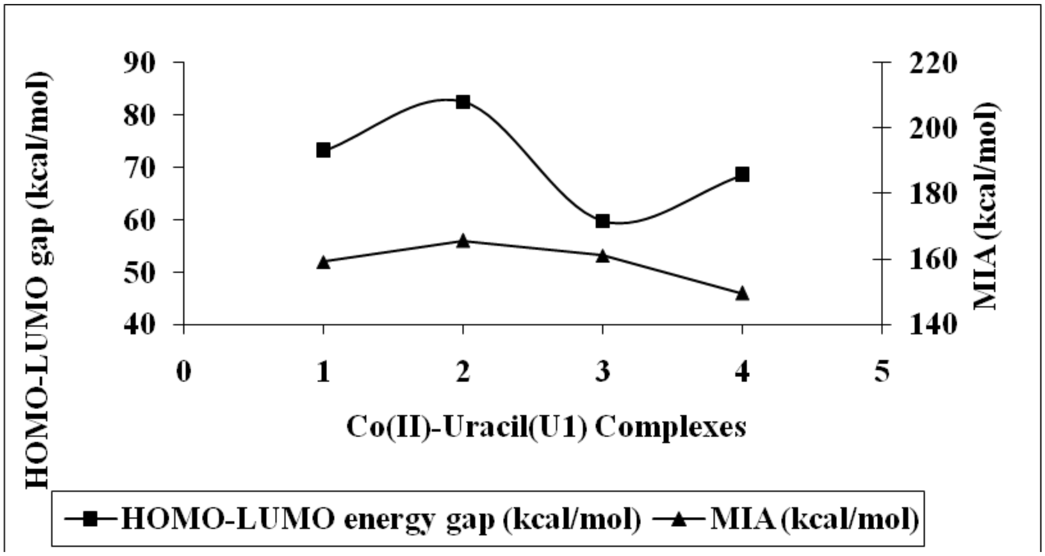


Fig. 13: Correlation between the MIA and the difference between the HOMO-LUMO energies of Co^{2+}-Uracil complexes

CONCLUSION

- i) Both Co^{2+} and Fe^{2+} undergo complexation with uracil at O-atoms. However modes of attachments are different. Metallation at N5 and N7 leads bi coordinated complexes in either case.
- ii) O1 atom of Uracil serves as the most preferred cite of complexation during the attachment of Fe^{2+} on, while N7 atom serves as the site with the highest metal ion affinity during the attachment of Co^{2+} ion.
- iii) In the case of Co^{2+}-Uracil complex, the complex with the highest HOMO-LUMO energy gap is seen to possess the highest MIA, however similar correlation is not seen during the complexation with Fe^{2+} ion.
- iv) In all complexes, highest accumulation of negative charge is seen at the site of attachment of metal ion. It can occur in two instance, either due back bonding i.e by the donation of electrons by the metal ion to the vacant orbital of the basic site, which is not possible in the present case, since either N or O atoms do not have any vacant orbital for receiving electrons. The other reasonable possibility is the flow of electrons towards the positively charged metal ion from nearby electron rich sites as a result of +M effect.
- v) The lower values of retained charges on metal atoms in Co^{2+}-Uracil complexes indicates higher charge transfer in Co^{2+}-complexes than that in Fe^{2+}-complexes

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REFERENCES

1. Sponer JE, Sychrovsky V, Hobza P and Sponer. J Phys Chem Chem Phys. 2004;6:2772-2780.
2. Siegel A and Siegel H. Metal ions in biological systems. Marcel Decker Inc., New York. 1996:32.
3. Sponer JE, Burda VJ, Leszczynki J and Sponer. Computational studies of RNA and DNA. Chapter 15, 389-410.
4. Russo N, Marino T, Toscano M and Grand A. Int J Quant Chem. 2004;98:347.
5. Russo N, Toscano M and Grand A. J Mass Spectrum. 2003;38:265.
6. Russo N, Toscano M and Grand A. J Am Chem Soc. 2001;123:10272-10279.
7. Zhu WL, Jiang HL, Puah CM, Tan XJ, Chen KX, Cao Y and Ji RY. J Chem Soc Perkin Trans. 1999;2:2615.
8. Marino T, Mazzuca D, Russo N, Toscan M and Grand A. Int J Quant Chem. 2010;110:138-147.
9. Russo N, Sicilia E Toscano M and Grand A. Int J Quant Chem. 2002;90:903.
10. Parr RG and Yang W. Density Functional Theory of atoms and molecules. Oxford University Press. Oxford, UK, 1989.
11. Parajuli R. Acta Chim Pharm Indica. 2012;2(2):85-94.
12. Parajuli R. Int J Chem Sci. 2012;10(3):1477-1486.
13. Frisch MMJ et al. *Gaussian* 94; Gaussian Inc, Pittsburgh PA. 1995.
14. Russo N, Toscano M, Grand A and Jolibois F. J Comp Chem. 1998;19:9:989-1000.