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

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ABSTRACT

Co^{2+}-Adenine and Fe^{2+} -adenine complexes were studied at all possible basic sites of adenine using DFT method. Interesting correlation exists between the MIA's and retained charges of metal ions. Extended study establishes another correlation between MIA and the HOMO-LUMO energy gap in adenine-(Fe^{2+}/Co^{2+}) complexes. The study shows that Co^{2+}-adenine complexes are more stable than corresponding Fe^{2+}-adenine complexes.

Key words: DFT, Adenine, Metal ion affinity, Mulliken Net Charges, Bond lengths, HOMO-LUMO energies.

INTRODUCTION

The importance of metal ion binding with nucleic acid has been studied widely for its vast importance in explaining the neutralization of charges of nucleic acids as well as for their importance in many essential biological functions.[1-2] Such interactions are common with Na^+, K^+, Mg^{2+}, Ca^{2+} etc. alkali and alkaline earth metal ions. These metal ions are reported to interact with DNA in two possible ways. Sometimes they interact with the phosphate group of DNA backbone and in other times they interact with the nitrogeneous base of DNA, however, the contribution of the first type interaction is more dominating. Such interactions, which are mostly electrostatic in nature stabilize the DNA double helix[3-4].

Recently, DFT based quantum chemical techniques have emerged as an important mean for the theoretical studies of metal ion–nucleic acid interactions[5]. Russo and Toscano[6] carried out numerous studies on the interaction of various metal ions with nucleic acid bases, amino acids etc. in the gas phase using DFT methods. Trends of theoretical results obtained were in agreement with experimental findings with differences well within acceptable

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limits[6-10]. Computational methods give an idea about the resultant structure, stability, thermodynamic and electronic properties of the complex system, which in turn helps in the understanding of biological functions. Of course the limitations of gas phase data while correlating with the complex physiological conditions of nucleic acids cannot be under estimated.

In the present study, we have carried out detailed computations for the interaction of Fe^{2+} and Co^{2+} ions with adenine using density functional theory methods [11]. 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. Our previous works suggest that there exist some interesting correlation between the HOMO-LUMO energy gap and the stability of metal-base complexes[16-19]. So, here also an attempt is made to correlate the stabilities of different complexes with the energies of the frontier orbitals.

Computational details

All necessary computations were done using the Gaussian 09 (G09W) programme. All geometries of adenine and adenine-(Fe^{2+}/Co^{2+}) complexes were optimized using Becke3 (B3) exchange[20] and Lee et al.[21] correlation potentials with 6-31G** basis sets as incorporated in Gaussian 09' code in the gas phase. Density functional theory method with B3LYP functional is used in the study of various metal ion-heteroatom complexes. Metal ion-π interaction was ignored as the interaction will not be favorable with adenine as per literature[22]. With a view to correlate between the metal ion affinity (MIA) and the charge transfer in complexes, MIA's are calculated assuming that they are negative of the enthalpy change (ΔH) for the process.

$$\text{Adenine} + Fe^{2+}/Co^{2+} \rightarrow \text{Adenine-}(Fe^{2+}/Co^{2+})$$

It can be also be calculated as –

$$\text{MIA} = [E^0\,(\text{Adenine} - (Fe^{2+}/Co^{2+})\ \text{complex}] - E^0\,(Fe^{2+}/Co^{2+}) - E^0\,(\text{Adenine})$$

Here E^0 represents absolute energies of molecules and ions. HOMO LUMO energies as well as Mulliken net charges of the atoms are extracted from the optimized geometries of complexes using the same basis sets.

RESULTS AND DISCUSSIONS

Works of Russo et al.[23] suggested that out of the following three possible tautomers of adenine the first one i. e. A1 is prevalent because rest two tautomers are separated by more than 8 kcal/mol energy from A1.

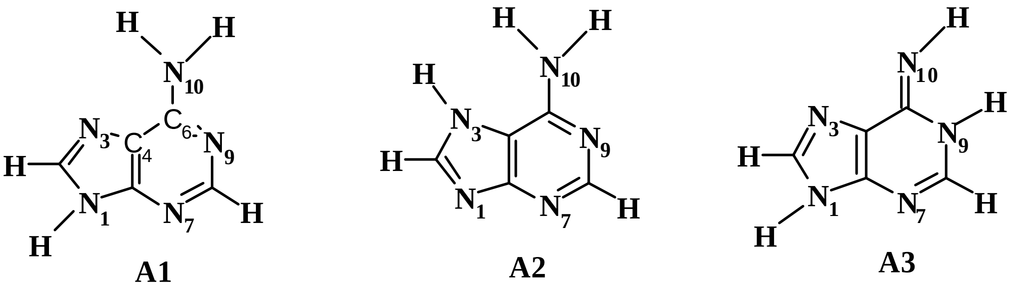

Fig. 1: Three stable tautomers of Adenine. (Positions of N atoms are given as per their positions in the metal ion-Adenine complexes)

Adenine complexes of Fe^{2+}/Co^{2+} at all the nucleophillic sites of adenine are optimized, to see the preferred co ordination site of metal ions with A1 using G09W programme. Optimized structures of Fe^{2+}-adenine complexes are shown in Figs. 2(a)-2(e) while those of Co^{2+}-adenine complexes are shown in Figs. 2(f)-2(j). It is seen from the table 1 that both; in the cases of Fe^{2+} and Co^{2+} -adenine complexes the interaction at N10 position has the highest metal ion affinity (MIA) value. Their corresponding optimized structures in Figs 2(e) and 2(j) show that in either case there is ring formation after complexation with metal ion and the chelation accounts for the high MIA values as compared to other complexes. MIA values of Co^{2+}-adenine complexes are more than those of Fe^{2+}-adenine complexes for metallation at each possible nucleophillic site of adenine.

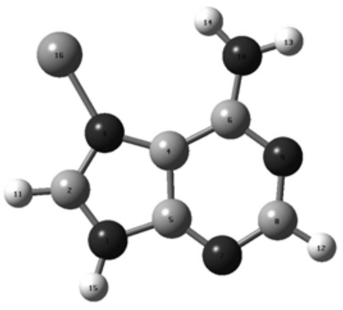

Fig. 2(a): Fe^{2+}-Adenine (N1) complex

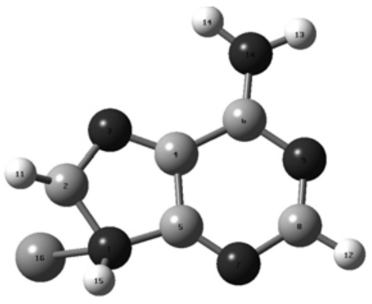

Fig. 2(b): Fe^{2+}-Adenine (N3) complex

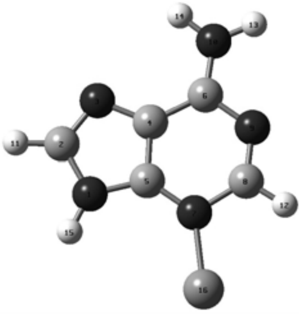

Fig. 2(c): Fe^{2+}-Adenine (N7) complex

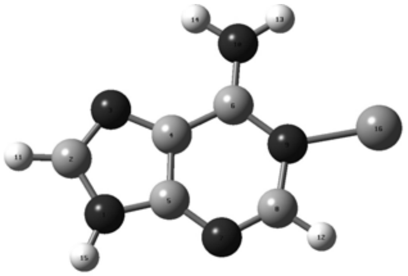

Fig. 2(d): Fe^{2+}-Adenine (N9) complex

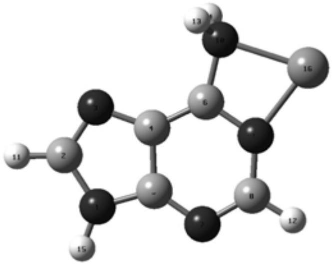

Fig. 2(e): Fe^{2+}-Adenine (N10) complex

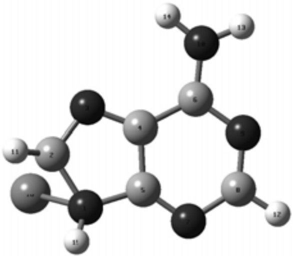

Fig. 2(f): Co^{2+}-Adenine (N1) complex

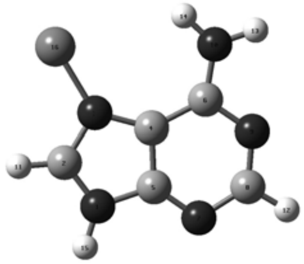

Fig. 2(g): Co^{2+}-Adenine (N3) complex

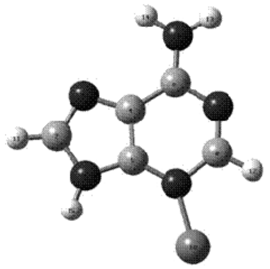

Fig. 2(h): Co^{2+}-Adenine (N7) complex

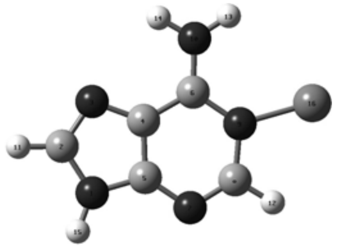

Fig. 2(i): Co^{2+}-Adenine (N9) complex

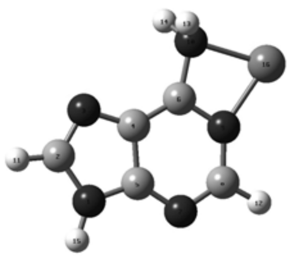

Fig. 2(j): Co^{2+}-Adenine (N10) complex

In the Table 2, Mulliken net charges at the site of attachment of metal ion and its nearby sites are given to explore the effect of metalation on the overall electron distribution in the metal ion-nucleic acid complex. All the results are extracted from the optimized geometries after calculation at B3LYP/6-31G** level. Thus, Table 2 provides the retained charges on metal atoms as well as resultant charges of N atoms in the Fe^{2+}/Co^{2+}-adenine complexes. It is seen that the magnitude of retained charge of either metal atom is the highest in the case of M^{2+}-Adenine (N10) complex and lowest in the cases of M^{2+}-Adenine (N1) complexes. Both metal atoms show the identical trend of the variation of the retained charges on N atoms from N1 to N10 complexes. Very interesting results emerge while correlating the results of Table 1 and 2. It is seen that the values of MIA's increase with increasing retained charge on metal atoms. The correlation is clearer in Figs. 3(a) and 3(b), in which we have plotted MIA's as well as retained charges of metal atoms for all metal ion-adenine complexes. Magnitudes of retained charges on metal atoms in Fe^{2+}-adenine complexes at each complexation site is more than those in the cases of Co^{2+}-adenine complexes. It justifies the higher metal ion affinities of Fe^{2+}-adenine complexes than Co^{2+}-adenine complexes. Figs. 2(i) and 2(j) show that in case of M^{2+}-adenine complexes there is a formation of a cyclic ring, which provides an additional stability to these complexes to account for their highest MIA values. B3LYP/6-31G** calculation of Co^{2+} and Fe^{2+} ions show that LUMO energies of the two ions are -0.7278 a.u. and -0.7058 a.u., respectively. The lower value of the LUMO energy of Co^{2+} ion suggests that charge transfer in Co^{2+} -adenine complex is easier than that in Fe^{2+}-adenine complex. It accounts for the lower values of retained charges on Co-atoms in Co^{2+}-adenine complexes as compared to those in Fe^{2+}-adenine complexes. More charge transfer from the nucleophillic N atoms to metal ions causes dispersal of their positive charges more. Greater neutralization of positive charge causes more heat to be released, which in turn accounts for the higher stability and hence MIA values of Co^{2+}-adenine complexes than Fe^{2+}-adenine complexes. Values of bond lengths of few selected bonds in the most stable metal ion-adenine complexes are given in Table 3 and are compared with the corresponding values in the free adenine base. Lengthening of 10N-6C bond in M^{2+}-adenine (N10) complexes are due to the charge transfers taking place in these complexes from N atoms to the respective metal ions. However, after metallation, the complex with the highest HOMO-LUMO gap will be regarded as the most stable complex. In Table 4, HOMO-LUMO energy gap (in kcal/mol) is reported for the optimized geometries. Higher such gap in the cases of Co^{2+}-adenine complexes indicates higher stabilities of Co^{2+}-complexes than Fe^{2+}-adenine complexes. In either complex, complexes with metal ions attached to N10 possess the highest HOMO-LUMO gap and hence are more stable. Figs. 4(a) and 4(b) show the possible correlation between the MIA and the HOMO-LUMO energy gap of Fe^{2+}/Co^{2+}-Adenine complexes. The plots establish the reverse correlation between the HOMO-LUMO energy gap and stability in terms of MIA values

Table 1: MIA's (B3LYP/6-31G) of different Adenine-(Fe^{2+} /Co^{2+}) complexes**

Fe^{2+}-adenine complex		**Co^{2+}-adenine complex**	
Position	**MIA (kcal/mol)**	**Position**	**MIA (kcal/mol)**
N1	142.8119	N1	168.2938
N3	160.6491	N3	187.6007
N7	172.3084	N7	199.6376
N9	168.7935	N9	192.5935
N10	193.4873	N10	216.4683

Table 2: Computed Mulliken net charges (Q/e) on various atoms of adenine- (Fe^{2+}/Co^{2+}) complexes

Complex	**Positions**	**Mulliken charge (Q/e)**	**Complex**	**Positions**	**Mulliken charge (Q/e)**
Fe-Adenine (N1)	N1	-0.6826	**Co-Adenine (N1)**	N1	-0.6631
	N3	-0.3654		N3	-0.3644
	N7	-0.4328		N7	-0.4265
	N9	-0.4278		N9	-0.4249
	N10	-0.5367		N10	-0.5310
	Fe	1.2098		Co	1.1554
Fe-Adenine (N3)	N1	-0.5064	**Co-Adenine (N3)**	N1	-0.5081
	N3	-0.8033		N3	-0.7887
	N7	-0.4374		N7	-0.4296
	N9	-0.4422		N9	-0.4364
	N10	-0.6002		N10	-0.5836
	Fe	1.2585		Co	1.1642

Cont…

Complex	Positions	Mulliken charge (Q/e)	Complex	Positions	Mulliken charge (Q/e)
Fe-Adenine (N7)	N1	-0.5888	**Co-Adenine (N7)**	N1	-0.5830
	N3	-0.4639		N3	-0.4625
	N7	-0.7759		N7	-0.7636
	N9	-0.4290		N9	-0.4278
	N10	-0.5495		N10	-0.5408
	Fe	1.2785		Co	1.1979
Fe-Adenine (N9)	N1	-0.5486	**Co-Adenine (N9)**	N1	-0.5447
	N3	-0.4837		N3	-0.4794
	N7	-0.4059		N7	-0.4065
	N9	-0.7903		N9	-0.7683
	N10	-0.5954		N10	-0.5812
	Fe	1.3055		Co	1.2155
Fe-Adenine (N10)	N1	-0.5484	**Co-Adenine (N10)**	N1	-0.5469
	N3	-0.4778		N3	-0.4756
	N7	-0.4163		N7	-0.4156
	N9	-0.7094		N9	-0.6955
	N10	-0.8119		N10	-0.7943
	Fe	1.3265		Co	1.2823

Table 3: Selected bond lengths (in Å) in the most stable Adenine-(Fe^{2+} /Co^{2+}) complexes obtained by B3LYP/6-31G calculation**

Fe-Adenine (N10)		Adenine
Bond	**Bond length (Å)**	**Bond length (Å)**
9N-16Fe	1.9657	-
6C-9N	1.3682	1.3449
8C-9N	1.3715	1.3434

Cont…

Fe-Adenine (N10)		**Adenine**
Bond	**Bond length (Å)**	**Bond length (Å)**
10N-16Fe	2.1014	-
6C-10N	1.4599	1.3558
7N-8C	1.3175	1.3369
Co-Adenine (N10)		**Adenine**
Bond	**Bond length (Å)**	**Bond length (Å)**
9N-16Co	1.9281	-
6C-9N	1.3687	1.3449
8C-9N	1.3707	1.3434
10N-16Co	2.0566	-
6C-10N	1.4596	1.3558
7N-8C	1.3177	1.3369

*Positions of carbon atoms in adenine-(Fe^{2+}/Co^{2+}) complexes complexes are shown in Fig. 1, A1

Table 4: Computed HOMO-LUMO energies (in kcal/mol) of different M^{2+}-adenine complexes

Complex	**HOMO energy (a.u.)**	**LUMO energy (a.u.)**	**HOMO-LUMO gap (Kcal/mol)**	**Complex**	**HOMO energy (a.u.)**	**LUMO energy (a.u.)**	**HOMO-LUMO gap (kcal/mol)**
Fe-Adenine (N1)	–0.5537	–0.4553	61.7032	Co-Adenine (N1)	–0.5599	–0.4556	65.4357
Fe-Adenine (N3)	–0.5316	–0.4586	45.8006	Co-Adenine (N3)	–0.5428	–0.4501	58.1212
Fe-Adenine (N7)	–0.5303	–0.4541	47.8457	Co-Adenine (N7)	–0.5388	–0.4484	56.7035
Fe-Adenine (N9)	–0.5299	–0.4631	41.9049	Co-Adenine (N9)	–0.5379	–0.4579	50.1668
Fe-Adenine (N10)	–0.5622	–0.4484	71.4016	Co-Adenine (N9)	–0.5656	–0.4521	71.2385

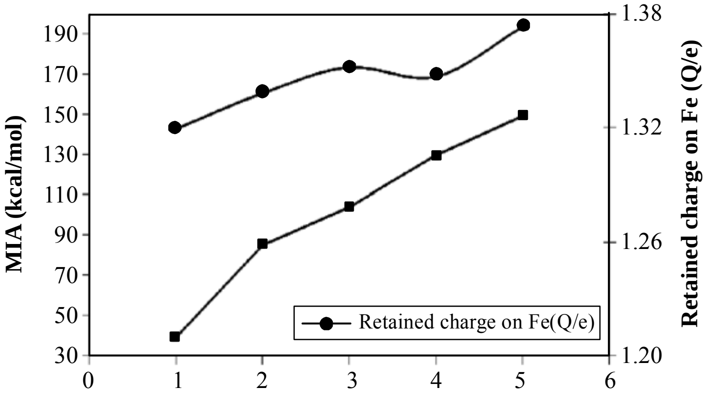

Fig. 3(a): Correlation between the MIA (in kcal/mol) and retained charge (Q/e) of Fe

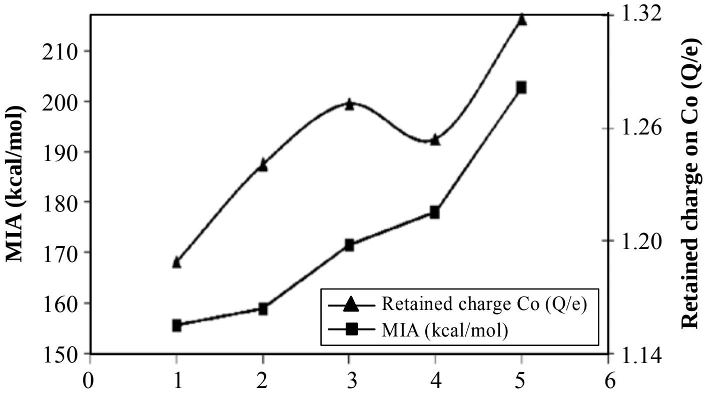

Fig. 3(b): Correlation between the MIA (in kcal/mol) and retained charge (Q/e) of Co

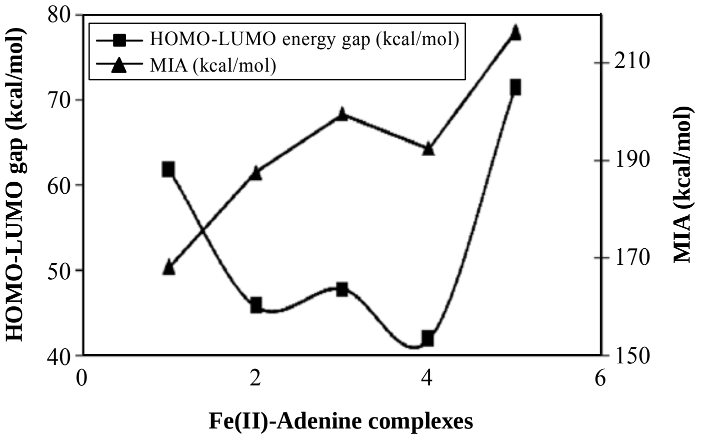

Fig. 4(a): Correlation between the MIA and the HOMO-LUMO energy gap of Fe^{2+}-Adenine complexes

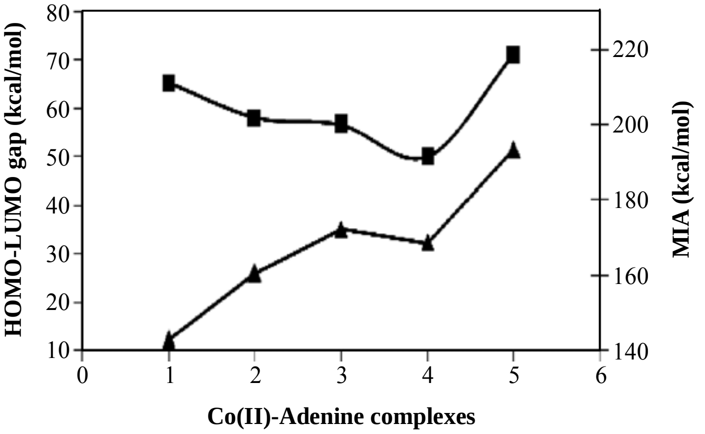

Fig. 4(b): Correlation between the MIA and the HOMO-LUMO energy gap of Co^{2+}-Adenine complexes.

CONCLUSION

(i) Both Fe^{2+} and Co^{2+} ions produce stable complexes with adenine at N10 position.

(ii) The trend of variation of MIA at various positions in the case of either metal ion-adenine complex is N10 > N9 > N7 > N3 > N1.

(iii) In either case the formation of the additional formation of cyclic ring increases the stability of metal ion-adenine (N10) complexes.

(iv) The variation of MIA's as well as stabilities can be correlated to the variation of charge transfer in complexes. Lower LUMO energy of Co^{2+} ion accounts for the more stable adenine complexes of Co^{2+} than those of Fe^{2+}.

(v) Most favorable complexation sites can be predicted on the basis of the HOMO-LUMO gap in various complexes without calculating MIA's because the two parameters are related inversely. A complex with higher HOMO-LUMO energy gap will have lower MIA or less stability. Lengthening of selected bond lengths as well as Mulliken net charges support the role of charge transfer data in predicting the stability of complexes.

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