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## Effects of platinum-cytosine complexes on watson crick pair: An ab initio, SCRF and isotropic NMR shielding tensor in gas phase

Robabeh Sayyadi\*, Hassan Kefayati

Chemistry Department, Islamic Azad University- Rasht Branch, P. O. Box -41335-3516, Rasht, (IRAN)

E-mail : sayyadi@iaurasht.ac.ir

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### ABSTRACT

The binding of Pt(II)-cytosine complex to Watson Crick GC pair of DNA were studied at the Hartree-Fock level of Theory. We used LANL2DZ basis set for atoms. Binding of Pt(II) at N7 of guanine actually could stabilize the Watson Crick GC pair. The gauge-invariant atomic orbital (GIAO) method was employed to calculate isotropic atomic shielding. SCRF calculations have proved useful in describing the effects of the solvent on some characteristics of the Platinum complexes in solution and have been performed at HF/LANL2DZ level. © 2010 Trade Science Inc. - INDIA

### KEYWORDS

Ab initio calculation;  
NMR shielding tensor;  
Binding energy;  
Pt(II)-DNA complexes.

### INTRODUCTION

In double-stranded DNA, pairing between the complementary bases guanine (G) and cytosine (C) as well as adenine (A) and thymine (T) is predominantly according to the Watson Crick fashion (Figure 1). This pairing scheme allows for anti parallel strand orientation (aps-DNA) in A, B and Z DNA.

The binding of metal complexes to DNA bases has been the subject of extensive experimental and theoretical studies in recent years after the discovery of the antitumor activity of *cis*-diamminedichloroplatinum(II) (*cis*-DDP or *cis*platin)<sup>[1,2]</sup>. The N7 sites of G and A, located in the major groove of double stranded DNA, are preferred metal binding sites. Amongst others, the antitumor agent *cis*-[PtCl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>] (*cis*platin) binds to these positions<sup>[3]</sup>.

Computational chemistry have allowed for extensive applications of reliable quantum chemical ap-

proaches to the investigation of interactions between metal cations and components of biomolecules including nucleic acid bases, base pairs and fragments<sup>[4-15]</sup>.

In our present study, we perform comprehensive ab initio quantum chemical study of the binding of Pt(II)-Cytosine complex to the N7 site of G in the Watson Crick guanine-cytosine (GC) pairs of DNA. The calculations were carried out at the Hartree-Fock level of Theory. We applied LANL2DZ basis set for atoms. The gauge-invariant atomic orbital (GIAO) method<sup>[16]</sup> was employed to calculate isotropic atomic shielding. Self-Consistent Reaction Field (SCRF) calculations have been used for describing the effects of solvent on some characteristics of the Platinum complexes in solution.

### Computational details

The optimized geometries of all systems were obtained using the framework of the Hartree-Fock (HF)

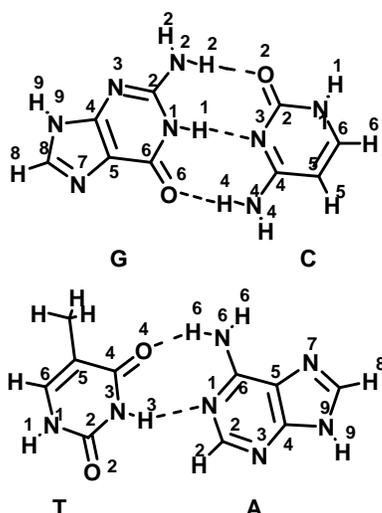


Figure 1 : Complementary Watson- Crick AT and GC base pairs and atom numbering scheme of nucleobase

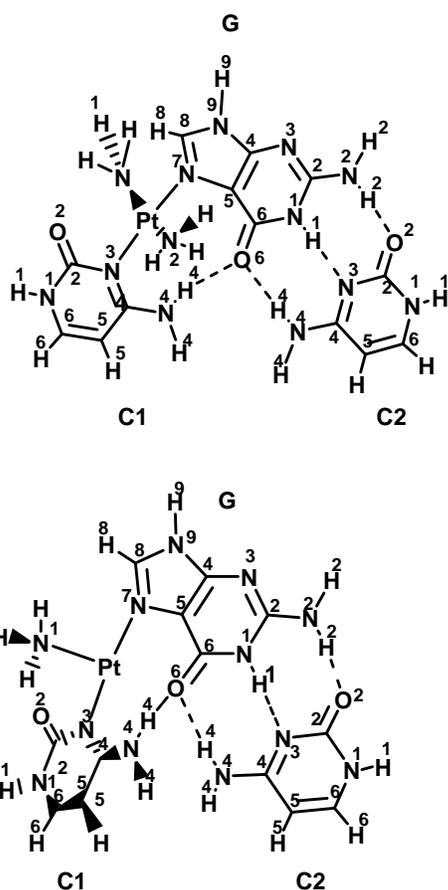


Figure 2 : Optimized structure of trans-Pt(NH<sub>3</sub>)<sub>2</sub> G C1C2 and Pt(NH<sub>3</sub>)<sub>2</sub> C1GC2 complexes in the HF/LANL2DZ

level of Theory. HF calculations are carried out with LANL2DZ basis set<sup>[17,18]</sup> using the Gaussian 98 series of program<sup>[19]</sup> on personal computer.

TABLE 1 : Optimized bond length and hydrogen bond length (Å) of platinum complexes and Watson Crick GC in HF/LANL2DZ

Bond length	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2	GC2
Pt-N7(G)	2.06	2.10	
Pt-N3(C1)	2.09	2.10	
Pt-N1(NH <sub>3</sub> )	2.11	2.08	
Pt-N2(NH <sub>3</sub> )	2.11		
N1-H1(G)	1.03	1.03	1.02
N2-H2(G)	1.00	1.01	0.99
C6-O6(G)	1.01	1.00	1.00
C6-O6(G)	1.27	1.30	1.24
N4-H4(C2)	1.00	1.00	1.01
C4-N4(C2)	0.99	0.99	0.99
C4-N4(C2)	1.34		
N4-H4(C1)	1.00	1.00	
N4-H4(C1)	1.00	1.00	
C2-O2(C2)		1.24	1.24
O6(G)...N4(C2)	2.10	2.10	1.98
N1(G)...N3(C2)	1.91	1.75	1.93
N2(G)...O2(C2)	1.73	1.71	1.91
O6(G)...N4(C1)	2.07	2.18	

TABLE 2 : Optimized bond angles of platinum complexes at LANL2DZ basis set

Bond angles	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2
N7-Pt-N1	87.99	95.23
N7-Pt-N2	92.20	
N3-Pt-N1	91.16	91.11
N3-Pt-N2	88.93	

NMR analysis has been performed using LANL2DZ basis set at the HF level. The GIAO methods were used to calculate the isotropic NMR shielding at the HF/LANL2DZ of theory.

The interaction energies of the counterparts were estimated as the energy difference between the complex and the isolated components and were corrected for the basis set superposition error (BSSE). The Boys-Bernardi Counterpoise Method<sup>[20,21]</sup>, applied at the Platinum-Cytosine complex on Watson Crick pair GC geometry, is used to account for BSSE. According to this method:

$$E_{\text{Corr}} = E_{\text{Interaction}} + \Delta E_{\text{BSSE}}$$

where  $E_{\text{Corr}}$  is corrected-interaction energies and

$$\Delta E_{\text{BSSE}} = [E_{\text{Pt-C}}^* - E_{\text{Pt-C}}(\text{Complex})] + [E_{\text{GC}}^* - E_{\text{GC}}(\text{Complex})]$$

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TABLE 3 : Thermochemistry analysis of the platinum complexes at HF/LANL2DZ level

	E (kcal/Mol)		CV (Cal/Mol-Kelvin)		S (Cal/Mol-Kelvin)	
	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2
Total Thermal	293.30	264.56	101.75	93.60	184.33	173.76
Electronic	0.00	0.00	0.00	0.00	0.00	0.00
Translational	0.89	0.89	2.98	2.98	45.070	44.98
Rotational	0.89	0.89	2.98	2.98	37.24	36.83
Vibrational	291.52	262.78	95.78	87.64	102.02	91.95

where E\* indicates that the energy of components at complex geometry calculated of Methods/Basis set of complex geometry.

The solvent effect is taken into account via the SCRF method. This method is based on Onsager reaction field theory of electrostatic solvation. In this model, the solvent is considered as a uniform dielectric with a given dielectric constant. The solute is placed into a cavity within the solvent. SCRF approaches differ in how they define the cavity and the reaction field. Thomasiões Polarized Continuum Model (PCM)<sup>[22]</sup> defines the cavity as a union of a series of interlocking atomic spheres.

## RESULTS AND DISCUSSION

The structures of Pt(II) complexes with the Watson Crick GC base pairs were optimized using the HF/LANL2DZ. The optimized structures (Pt(II) complexes) are presented in figure 2. The most important structural parameters of these complexes are reported in TABLE 1 and 2.

The geometry of the GC moiety was identical to the optimized geometry of the GC pair. The lengths of the Pt(II)-N7 and Pt(II)-N3 bonds were equal to 2.06 and 2.09 Å in the Pt(NH<sub>3</sub>)<sub>2</sub>C1GC2 and 2.10 and 2.10 Å in the Pt(NH<sub>3</sub>)C1GC2. The bond angles of N7-Pt-N in Pt(NH<sub>3</sub>)<sub>2</sub>C1GC2 and N3-Pt-N in Pt(NH<sub>3</sub>)C1GC2 at distances ranging from 87 to 92, the above amounts were in agreement with the similar complexes systems of experimental results<sup>[23-26]</sup>. These results shown that the N7 site on guanine is a preferred site.

In the HF-SCF study, It was found that in the metalated Watson Crick GC base pair the H-bonding N1(G)...N3(C2) and N2(G)...O2(C2) distances decrease while the H-bonding O6(G)...N4(C2) distances increase (TABLE 1).

The PtCl<sub>4</sub><sup>2-</sup> complex, on the other hand, has D<sub>4h</sub> symmetry but owing to the loss of this symmetry in Platinum complexes, X-Pt-Y (X, Y=N7(G), N3(C) or N7(G), N(NH3)) angles differ from the ideal value of 90°. The bond angles of N7(G)-Pt-N1 and N7(G)-Pt-N2 are 87.99 and 92.20, respectively and the angles of N3-Pt-N1 and N3-Pt-N2 in the Pt(NH<sub>3</sub>)<sub>2</sub>C1GC2 complex are 91.16 and 88.93, respectively as seen in Figure 2. These results show the existence of hydrogen bond interaction between the O6 guanine and H4 (N4H)-C1. These data imply that Pt(II) binding to N7 guanine acidifies the proton at N1 and N2, thereby facilitating deprotonation of this site. On the other hand, this binding causes acidity of N1H and N2H on guanine increased and basicity O6 decreased.

The computed stabilization energies (Hartree) of Pt(NH<sub>3</sub>)<sub>2</sub>C1GC2, Pt(NH<sub>3</sub>)C1GC2 and GC2 in gas phase with HF/LANL2DZ level are -1554.59, -1498.36 and -931.76, respectively. Therefore, increasing of coordination number of Pt(II) complex and binding of Pt(II) to N7 of guanine increase the stability of the Watson Crick base pair. Zero point energy (Hartree) for the Pt(NH<sub>3</sub>)<sub>2</sub>C1GC2 and Pt(NH<sub>3</sub>)C1GC2 are -1554.15 and -1497.96, respectively. These results and thermo chemistry analysis are shown that Pt(NH<sub>3</sub>)<sub>2</sub>C1GC2 complex is stable than the Pt(NH<sub>3</sub>)C1GC2 complex (TABLE 3). The data of TABLE 3 is accepted into following equation:

$$E_{\text{Total}} - E_0 = E_{\text{Rot}} + E_{\text{Trans}}$$

To check whether BSSE can significantly influence the result, we also employ an ab initio BSSE-free method. TABLE 4 shows the value of BSSE and E<sub>1+BSSE</sub> for the structures. Clearly, for the all complexes, the values of BSSE are rather small and is negligible.

The NMR shielding tensors were calculated using GIAO method at HF/LANL2DZ level. The isotropic part  $\sigma_{\text{iso}}$  of  $\sigma$  is measured by taking the average of  $\sigma$

**TABLE 4 :**  $E_1$  (Interaction energies), BSSE and  $E_{1+BSSE}$  (Hartree) for complexes at HF/LANL2DZ level

Complex	$E_1$	$E_{1+BSSE}$	BSSE
Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	-0.8298	-0.8381	-0.0083
Pt(NH <sub>3</sub> )C1GC2	-0.8897	-0.8990	-0.0093

**TABLE 5 :** Relative (to TMS) shifts in ppm for <sup>13</sup>C-NMR of Pt-complexes using GIAO method at HF/LANL2DZ. TMS: isotropic hydrogen shielding tensor= 33.62 at HF/LANL2DZ and GIAO method

Atom	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2	GC2
H1(N <sup>1</sup> H <sub>3</sub> )	0.49		
H2(N <sup>1</sup> H <sub>3</sub> )	0.12		
H3(N <sup>1</sup> H <sub>3</sub> )	2.87		
H1(N <sup>2</sup> H <sub>3</sub> )	0.34	3.48	
H2(N <sup>2</sup> H <sub>3</sub> )	-0.18	-0.16	
H3(N <sup>2</sup> H <sub>3</sub> )	2.97	-0.04	
H1(C1)	8.22	8.01	
H6(C1)	9.13	8.86	
H5(C1)	6.83	6.56	
H4(N <sup>4</sup> H <sub>2</sub> in C1)	5.59	5.72	
H4(N <sup>4</sup> H <sub>2</sub> in C1)	8.85	6.90	
H9(G)	8.95	8.71	7.34
H8(G)	8.76	8.47	8.17
H1(G)	14.99	15.78	13.53
H2(NH <sub>2</sub> in G)	11.60	11.31	8.64
H2 (NH <sub>2</sub> in G)	6.32	6.64	4.63
H1(C2)	7.95	8.01	6.69
H6(C2)	8.84	8.86	8.08
H5(C2)	6.68	6.56	6.28
H4(NH <sub>2</sub> in C2)	4.55	4.19	4.70
H4(NH <sub>2</sub> in C2)	7.73	6.01	11.04

with respect to the orientation to the magnetic field, i.e.,  $\sigma_{iso} = (\sigma_{11} + \sigma_{22} + \sigma_{33})/3$ . The results calculated are summarized in TABLE 5 and 6.

Ab initio calculations yield the data in TABLE 5 and 6 show that the values for the chemical shifts to TMS of the H1(G) and H2( H-bonding NH<sub>2</sub> in G) atoms for metalated Watson-Crick GC are larger than nonmetalated while H4(H-bonding NH<sub>2</sub> in C2) and N7(G) ( to NH<sub>4</sub><sup>+</sup>) atoms in the metalated Watson-Crick GC have been decreased.

The effect of solvent on the Platinum complexes show that with the increase of dielectric constants of solvent, the polar solute-solvent intraction has been in-

**TABLE 6 :** Relative (to NH<sub>4</sub><sup>+</sup>) shifts in ppm for <sup>15</sup>N-NMR of Pt-complexes, using GIAO method at HF/LANL2DZ. The <sup>15</sup>N-NMR chemical shift ( $\delta = \sigma_{iso}^{TMS} - \sigma_{iso}^{Sample}$ ). NH<sub>4</sub><sup>+</sup>: Isotropic nitrogen shielding tensor= 258.4809 at HF/LANL2DZ and GIAO method

Atom	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> )C1GC2	GC2
N1(NH <sub>3</sub> )	-38.39		
N2(NH <sub>3</sub> )	-41.10	-59.38	
N1(C1)	127.03	126.16	
N4(C1)	82.85	86.79	
N3(C1)	134.43	125.67	
N9(G)	149.66	146.21	137.73
N7(G)	175.41	176.21	318.09
N1(G)	144.31	141.31	143.54
N2 (NH <sub>2</sub> in G)	85.55	89.57	61.66
N3(G)	185.71	199.56	175.32
N1(C2)	128.52	129.02	122.28
N4(C2)	72.05	71.13	87.79
N3(C2)	210.63	207.52	210.30

**TABLE 7 :** Polar solute-solvent (kcal/mol) and for complexes of the platinum invarious solvent in HF/LANL2DZ

Solvent	Pt(NH <sub>3</sub> ) <sub>2</sub> C1GC2	Pt(NH <sub>3</sub> ) C1GC2
Cyclohexane	-65.48	-65.37
Chloroform	-106.63	-105.69
Dichloromethane	-120.59	-119.36
Acetone	-130.37	-128.95
Acetonitrile	-133.97	-132.40
DMSO	-134.72	-133.04
Water	-137.22	-135.70

creased. This shows that the Platinum complexes are polar. The stability of the Platinum complexes increased by decreasing of the dielectric constant.

## CONCLUSION

The results of calculations were carried out at the Hartree-Fock level with LANL2DZ basis set were agreement with the similar complexes systems of experimental data and show that Pt binding to N7 site guanine of GC base pair causes significant changes in the interaction between guanine and cytosine compared to the Watson Crick H-bonding pattern. This obtained data for model systems in our work have shown that the N7 site on guanine are preferred metal binding site and suggest that Pt(II) at N7 of guanine could actually

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stabilize the Watson Crick GC pair. The obtained data from ab initio calculation and NMR shielding tensors using the GIAO method and HF/LANL2DZ level, imply that the opposing effects of increased N1H and N2H acidities and reduced O6 basicity lead to a net increase in H-bonding affinity between N7 platinated G and the complementary base C.

SCRF calculations on Platinum complexes show that the polar solute-solvent interaction in different solvent have been increased with the increase of dielectric constants and the stability of the Platinum complexes decrease with the increasing polarity of solvent.

### ACKNOWLEDGEMENTS

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### REFERENCES

- [1] S.Mansy, B.Rosenberg, A.J.Thomson; *J. Am. Chem.Soc.*, **95**, 1633 (1973).
- [2] B.Rosenberg; *Biochem.*, 859 (1995).
- [3] G.Schroder, M.Sabar, I.Baxter, J.Kozelka, B.Lippert; *Inorg.Chem.*, **36**, 490 (1997).
- [4] J.Bertran, L.Rodrigues-Santiago, M.Sodupe; *J.Phys.Chem.B*, **103**, 2310 (1999).
- [5] L.Ruhsek, Z.Havias; *J. Am. Chem. Soc.*, **122**, 10428 (2000).
- [6] G.Tiraboschi, B.P.Roques, N.Gresh; *J. Comput.Chem.*, **29**, 1379 (1999).
- [7] L.Ruhsek, Z.Havlas; *J.Phys.Chem.A*, **103**, 1634 (1999).
- [8] A.Luna, S.Geveyer, J.Tortajada; *J.Phys.Chem.B*, **104**, 110 (2000).
- [9] J.Sponer, M.Sabat, J.Burda, J.Leszczynski, P.Hobza, B.Lippert; *J.Biol.Inorg.Chem.*, **4**, 537 (1999).
- [10] J.Sponer, J.E.Sponer, L.Gorb, J.Leszczynski, B.Lippert; *J.Phys.Chem.A*; **103**, 11406 (1999).
- [11] I.L.Zilberberg, V.I.Avdeev, G.M.Zhidomiror; *J.Mol.Struct.(Theochem)*, **418**, 73 (1997).
- [12] J.Sponer, J.Burda, J.Leszczynski, P.Hobza; *J.Biol.Struct.Dyn.*, **17**, 61 (1999).
- [13] C.F.Guerra, F.M.Bickelhaupt, J.G.Snijders, E.J.Baerends; *J. Am. Chem. Soc.*, **122**, 4117 (2000).
- [14] V.V.Murashov, J.Leszczynski; *J.Phys.Chem.B*, **103**, 8391 (1999).
- [15] A.Famulari, F.Moroni, M.Sironi, M.Raimondi; *J. Comput.Chem.*, 24341 (2000).
- [16] K.Wolinski, J.F.Hilton, P.Pulaj; *J. Am. Chem. Soc.*, **112**, 8251 (1990).
- [17] P.C.Hariharan, J.A.Pople; *Theor.Chim.*, **28**, 213 (1973).
- [18] B.A.Hathaway, G.Day, M.Lewis, R.Glaser; *J.Chem.Soc.Perkin Trans*, **2**, 2713 (1998).
- [19] M.J.Frisch; 'Gaussian 98 Revision A.', Gaussian: Pittsburgh PA, 7 (1998).
- [20] J.R.Cheeseman, M.J.Frisch, G.W.Trucks, T.A.Keith; *J.Chem.Phys.*, **104**, 5497 (1996).
- [21] F.S.Boys, F.Bernardi; *Mol.Phys.*, **19**, 553 (1970).
- [22] J.R.Hanson, M.D.Liman, C.Uyanik; *J.Chem.Research(s)*, 126 (1998).
- [23] J.P.Caradonna, S.J.Lippard, M.Gait, M.Singh; *J. Am. Chem. Soc.*, **104**, 5793 (1982).
- [24] P.Pelmenschikov, I.Zilberberg, J.Leszczynski, A.Famulari, M.Sironi, M.Raimondi; *Chem.Phys. Lett.*, **314**, 496 (1999).
- [25] N.Gresh, J.Sponer; *J.Phys.Chem.B*, **103**, 11415 (1999).
- [26] I.Dieter-Wurm, M.Sabat, B.Lippert; *J. Am. Chem. Soc.*, **114**, 357 (1992).