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Thermodynamic Parameters of Cis-Platin and Trans-Platin Complexes with Guanine in Water, A DFT Study

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ABSTRACT

The binding energy and Thermodynamic Parameters of *cis*- Platinum Di Ammino Chlorine (*cis*-[Pt(NH₃)₂Cl]⁺) and *trans*- Platinum Di Ammino Chlorine (*trans*- [Pt(NH₃)₂Cl]⁺) complexes with Guanine has been studied by density functional theory (DFT) calculations in water. The binding energies (E_{bin}) of *cis*- and *trans*-[Pt(NH₃)₂ClG]⁺ are calculated to be 79.38 kcal/mol and 74.98 kcal/mol, respectively. The binding energy (E_{bin}) of *cis*-[Pt(NH₃)₂ClG]⁺ turns out to be energetically more favorable by about 1.88 kcal/mol than the *trans*-[Pt(NH₃)₂ClG]⁺. At the point of thermodynamic, the formation of *cis*-[Pt(NH₃)₂ClG]⁺_(aq) with Δ G (Solv) equal to -10.36 kcal/mol is more favorable than *trans*-[Pt(NH₃)₂ClG]⁺_(aq) with 16.21 kcal/mol.

Keywords: cis-Pt; trans-Pt; Guanine; Binding Energy; Thermodynamic Parameters

INTRODUCTION

Cis-platinum is used as a popular remedy against a variety of solid tumors to chemotherapy. Despite the considerable success, it has been achieved several restrictions. The search for similar drugs that are covered by these shortcomings, carbo-platin and cis-platin resulted in cross linking within between interdisciplinary part of the complex of platinum (II) and the N_7 atom of the purine DNA formed. The binding of Pt(II) complexes to DNA bases has been the subject of extensive experimental and theoretical studies in recent years after the discovery of Rosenberg et al. of the antitumor activity of cis-diammine dichloro platinum(II) (cis-DDP or *cis*-platin) [1, 2]. The many results

COMPUTATIONAL METHODS

In the present work, we describe

of investigation have shown that *cis*-platin attacks DNA base and it inhibits DNA replication [3]. The mono functional binding sites of the neutral base guanine have been investigated for the $Pt(NH_3)_2Cl^+$ (Platinum Di Ammino Chlorine PDAC)[4]. The results have shown that the N₇ site on guanine has been identified as a preferred site. Basch et al. have studied on binding of $Pt(NH_3)_3^{2+}$ to nucleic acid bases by *ab initio* calculation [5]. They have reported that the binding energy of N₇ site of the guanine is found to be greater than O_6 site.

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theoretically the connection of cis- and trans- isomers of PDAC to guanine at solvent. We consider monoaqua complex $[Pt(NH_3)_2Cl(H_2O)]^+$. In the results reported below, solution calculations were carried out at a dielectric constant of 80.37 for water. The N₇ site is considered for binding of guanine to PDAC. The minimum energy geometries of cis- and trans- isomers of PDAC, guanine, and PDAC complexes of guanine are optimized by density functional theory (DFT). DFT calculations are carried out at B₃lyp level of theory with the LANL2DZ basis set for Pt and 6-31G* for other atoms using the Gaussian 03 program [6].

Discussions

The optimized geometrical structure is shown in Figure 1 for the cis-PDAC with guanine complex $(cis-[Pt(NH_3)_2ClG]^+)$. The optimum $Pt-N_7(G)$ distance in the *cis*- $[Pt(NH_3)_2ClG]^+$ complex is found to be 2.200 Å. The optimized geometric structure is shown in Figure 2 for the trans-PDAC with guanine complex (trans- $[Pt(NH_3)_2ClG]^+$ that the optimum Pt- $N_7(G)$ distance is calculated to be 2.238 Å. The total energies for each compound and binding energies for $[Pt(NH_3)_2ClG]^+$ complexes are summarized in Table 1. As shown in Table 1, the *cis*-[Pt (NH₃)₂Cl]⁺ is calculated to be energetically more favorable by about 1.88 kcal/mol than the *trans*- $[Pt(NH_3)_2Cl]^+$. The isomeric energy may play a role in relative reactivity. On the other hand, it is found for the [Pt where $(NH_3)_2ClG]^+$, the transconformation (*trans*- $[Pt(NH_3)_2ClG]^{\top}$) is more favorable by about 2.51 kcal/mol than that of *cis*- $[Pt(NH_3)_2ClG]^+$, as can be seen in Table 1. We investigate the binding energy values in order to compare the binding strength of PDAC isomers to guanine. The binding energies (E_{bin}) of cisand *trans*- $[Pt(NH_3)_2ClG]^+$ are calculated to

be 79.38 kcal/mol and 74.98 kcal/mol in solvent, respectively, by Eq1.

$$E_{bin} = E_{[Pt(NH_3)_2ClG]_{aq}^+} - (E_{[Pt(NH_3)_2Cl]_{aq}^+} + E_{guanine_{aq}})$$
(1)

In the calculation, the E_{bin} of *cis*-[Pt(NH₃)₂ClG]⁺ turns out to be energetically more favorable by about 4.4 kcal/mol than that of E_{bin} of *trans*-[Pt(NH₃)₂ClG]⁺. The result obtained in this study suggests that the *cis*-PDAC bind more strongly to the guanine base than *trans*-PDAC.



Fig. 1. Optimized structure of cis-[Pt(NH₃)₂ClG]⁺.



Fig. 2. Optimized structure of *trans*-[Pt(NH₃)₂ClG]⁺.

The electrostatic interaction between the metal center and its closest atoms of the guanine is a magnitude subject. The molecular orbital interactions are unusually complicated. Intuitively, a donor-acceptor interaction between the N₇ lone-pair orbital of the guanine reactant and the empty Ptbased d_x^2 orbital is expected. These processes involve metal-based orbitals that are orthogonal to the molecular plane of the Pt fragment and have been said as π back-donation components of the Pt-N F. R. Nikmaram and M. Khan Ahmadi /J. Phys. Theor. Chem. IAU Iran, 10 (3): 211-214, Winter 2014

bond, implicating electron density flow from the metal center to the π^* -orbital of the guanine ring.

The vibrational frequency calculation results based on analytical second derivatives at the B3LYP/6-31G* level of theory were used to confirm proper convergence to local minima geometry and to derive the zero-point-energy (ZPE) and vibrational entropy corrections at room temperature. In the present work, we recommend using the value of 0.974 for scale factor to obtain accurate harmonic The frequencies [7]. thermodynamic properties in water were evaluated by a field (SCRF) self-consistent reaction approach [8,9]. The ZPE corrections, thermal corrections to the enthalpy, entropy terms, and continuum solution energies are added to give Gibbs free energies for the reaction in solution.

The entropy of solution is implicitly included in the solution free energy G (Solv) and cannot be separated when a continuum model is used.

Thus, it is convenient to introduce a new energy $\Delta H(Sol) = \Delta H(SCF) +$ $\Delta G(Solv)$, that is the electronic reaction energy as computed directly in the DFT calculation using the self-consistent-field procedure. All energy components are listed in Table2.

Reaction1: $cis-[Pt(NH_3)_2Cl]^+(aq)+$ Guanine $_{(aq)} \rightarrow cis$ - $[Pt(NH_3)_2ClG]^+_{(aq)}$

Reaction2: trans- $[Pt(NH_3)_2Cl]^+_{(aq)}$ + Guanine $_{(aq)} \rightarrow trans - [Pt(NH_3)_2ClG]^+_{(aq)}$

We found a more differential result of cis- $[Pt(NH_3)_2Cl]^+$ and trans- $[Pt(NH_3)_2Cl]^+$. At the point of thermodynamic, the formation of $cis-[Pt(NH_3)_2ClG]^+_{(aq)}$ with $\Delta G(Solv)$ equal to -10.36 kcal/mol is more favorable than *trans*- $[Pt(NH_3)_2ClG]^{+}_{(aq)}$ with 16.21 kcal/mol. Also, on the base of value of ΔH (Sol) in Table 2, the reaction 1 for cis-[Pt (NH₃)₂ClG]⁺_(aq), is more exothermal with -80.71 kcal/mol with respect to reaction 2 for trans- $[Pt(NH_3)_2ClG]^+$ (aq) with -1.12 kcal/mol in water.

We compare the partial charge at the

structure	Pt-N ₇ / Å	E _{total} / (a.u.)	[*] E _{relative} / kcal.mol ⁻¹	E _{bin} / kcal.mol ⁻¹	
$cis-[Pt(NH_3)_2Cl]^+$	-	-262.321		-	
trans-[Pt(NH ₃) ₂ Cl] ⁺	-	-262.318	1.882	-	
$cis-[Pt(NH_3)_2ClG]^+$	2.200	-804.880		79.38	
trans-[Pt(NH ₃) ₂ ClG] ⁺	2.238	-804.884	2.510	74.98	
*E	is different of total energy of two structures				

Table 1. Bond length, total Energy, relative Energy and binding Energy in solvent

ent of total energy of two structures C relative IS

structure	H(SCF)	G(Solv)	
$cis-[Pt(NH_3)_2Cl]^+_{(aq)}$	-434474.01	-59.84	
<i>trans</i> - $[Pt(NH_3)_2Cl]^+_{(aq)}$	-415027.86	-19.51	
Guanine (aq)	-340575.51	-27.21	
$cis - [Pt(NH_3)_2ClG]^+_{(aq)}$	-775119.87	-97.41	
<i>trans</i> - $[Pt(NH_3)_2ClG]^+_{(aq)}$	-755620.70	-30.50	
	$\Delta H(SCF)$	$\Delta G(Solv)$	$\Delta H(Sol)$
Reaction1	-70.35	-10.36	-80.71
Reaction2	-17.33	16.21	-1.12

Table 2. *Thermodynamic properties at 298k in solvent

*All energies are given in kcal.mol⁻¹.

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 C_6 -oxo group of optimized structures of the mono aqua complexes. The charge of oxygen at the oxo group is --0.33 0.35 and for cis- $[Pt(NH_3)_2ClG]^+_{(aq)}$ transand $[Pt(NH_3)_2ClG]^+(aq),$ respectively. As expected, the oxo group at cis- $[Pt(NH_3)_2ClG]^{+}(aq)$ is much а better hydrogen-bond acceptor than the $[Pt(NH_3)_2ClG]^{T}(aq),$ transand the interaction is stronger reflected in $\Delta G(Solv)$, Table2.

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