[Article] www.whxb.pku.edu.cn

含平面胺配体的反式二价钯配合物与 DNA 碱基的作用

张东东 周立新*
(暨南大学化学系, 广州 510632)

摘要: 含大的平面胺配体的二价钯金属配合物在当前的抗肿瘤药物设计中代表着一类具有重要发展前途的先导结构. 由于大的平面胺配体具有较大的空间位阻, 目前主要的问题是这类化合物能否和 DNA 碱基结合形成单功能和双功能加合物. 我们采用密度泛函理论和等电聚焦连续极化(IEF-PCM)溶剂化模型研究了 *trans*-$PdCl_2L_2$ (L: 2-羟基吡啶)的钯配合物与 DNA 碱基的作用. 该化合物与 DNA 形成单功能和双功能加合物反应的活化自由能均低于铂类抗肿瘤药. 所有反应在水溶液中均为放热反应. 结果表明, 这一大的平面胺配体不会阻碍该化合物与 DNA 碱基形成双功能加合物, 而且该化合物与 DNA 的单功能和双功能结合的速率会大于铂类化合物.

关键词: 密度泛函理论; 嘌呤碱基; 胞嘧啶; 抗癌; 过渡态
中图分类号: O641

Interaction of a *trans*-Palladium (II) Complex Containing Planar Amine Ligands with DNA Bases

ZHANG Dong-Dong ZHOU Li-Xin*
(Department of Chemistry, Jinan University, Guangzhou 510632, P. R. China)

Abstract: Palladium (II) complexes coordinated to large planar amine ligands represent a lead structure of considerable interest in current antitumor drug design. However, the question is whether these complexes can bind to DNA bases affording bifunctional adducts for great steric hindrance provided by the bulky ligands. We studied the interaction of the palladium (II) complex, $PdCl_2L_2$, where L was 2-hydroxypydridine, with DNA bases using density functional theory and combining with isoelectric focusing polarized continuum (IEF-PCM) solvation model. Activation free energies for the complex monofunctional and bifunctional binding to DNA bases were lower than those for platinum-based antitumor agents. All reactions under study were exothermic in aqueous solution. The results indicate that the large planar amine ligands in the palladium complexes do not hinder formation of bifunctional adducts with DNA bases, and the rates for monofunctional and bifunctional binding to DNA bases to be larger than those of platinum-based agents.

Key Words: Density functional theory; Purine base; Cytosine; Antitumor; Transition state

Cisplatin is one of the most successful drugs in cancer chemotherapy, but side effect and resistance seriously limit its clinical usage[1,2]. This motivates great efforts in searching for metallopharmaceuticals with better activity and lower toxicity. It has been established that palladium (II) complexes display similar coordination geometry to platinum (II) complex[3,4]. And recent studies demonstrate that palladium (II) complexes with adequate donor ligands have stronger antitumor activity and lower resistance factor than cisplatin, and palladium (II) complex with planar amine ligands[5–12] represents a lead structure of considerable interest.

The primary target for platinum-based drugs is genomic DNA. The N7 atom of purine bases is the main binding site, with guanine being preferred over adenine[13]. This binding first generates monofunctional adducts, which subsequently close by coordination to the N7 position of an adjacent purine to afford an intrastrand cross-link. The most notable ones are the 1,2-d(GpG), followed by 1,2-d(ApG)[14,15]. It has been established that the binding models of Pd(II) complexes binding to DNA bases

Received: July 30, 2009; Revised: August 31, 2009; Published on Web: October 16, 2009.
*Corresponding author. Email: tlzhou@jnu.edu.cn; Tel: +86-20-85220223

are similar to cisplatin[16,17].

Huq *et al*.[10] reported three palladium (II) complexes with planar amine ligands with the form: *trans* Pd(II)Cl_2L_2, code named TH5, TH6, and TH7, where L=3-hydroxypyridine, 2-hydroxypyridine, and 4-hydroxypyridine, respectively. Among the three *trans* palladium compounds, TH6 is found to be most tumor active. For these three complexes, monofunctional adducts with guanine were detected[10] but it is still dubious whether these Pd(II) complexes could further interact with DNA base affording bifunctional adducts. It has been speculated that the great steric hindrance provided by two planar amine ligands would hinder the formation of bifunctional adducts. High level computation study is complementary to experiment and offers a quantitative atomic level understanding of the palladium complexes binding to DNA base. The hydrated platinum drugs interacting with DNA bases[13,18–21] and other bio-relevant ligands[22–24] have been intensively studied. Herein, we studied kinetic and thermodynamic behaviors of TH6 interaction with DNA bases and compared to those platinum drugs.

The labeling of DNA bases and TH6 are following the convention as depicted in Fig.1. Two hydrated complexes: chloroaqua and diaqua of TH6 were considered as active species to form monofunctional adducts with guanine. Then monofunctional adduct of guanine of TH6 was employed as reactants to interact with guanine, adenine, and cytosine to form bifunctional adducts, respectively. For bifunctional adducts, there are mainly two conformations: the head to head (HH) in which hydrogen (H8) at C8 of both purine bases locate on the same side of palladium coordination plane for *trans*-Pd[GA]$^{2+}$ and *trans*-Pd[G]$_2^{2+}$, and the C═O of cytosine and guanine are arranged on the same side of the plane for *trans*-Pd[GC]$^{2+}$ adducts, and head to tail (HT) in which H8 of both purine bases are arranged on the opposite side of the plane for *trans*-Pd[GA]$^{2+}$ and *trans*-Pd[G]$_2^{2+}$, and the C═O of cytosine and guanine are located on the opposite side of the plane. Our objective of present study is mainly to explore kinetic behaviors of the selected Pd(II) complexes binding to DNA bases to form monofunctional and bifunctional products, especially from our analysis on transition states to predict whether reactions leading to bifunctional products are possible and analyze the role of hydroxyls on the pyridine-based ligands.

1 Computation details

The geometries of the molecules and transition states (TS) were optimized by B3LYP method[25,26], as implemented in Gaussian 03 program[27]. The LanL2DZ[28–30] effective core potential basis set was used for palladium atom and 6-31G(d,p) Pople basis set was used for all other atoms. Vibrational frequency calculations were based on analytical second derivatives on the same level of theory to confirm that the stationary point found was local minimum for reactant and product complexes and the first order saddle point for transition state and to derive the zero point vibration energy (ZPE) and vibrational entropy correction at room temperature. However, as we previously found that the ZPE contribution factors were similar in magnitude on reaction path and we did not include ZPE correction in our discussion on reaction energy profiles[18]. The reaction coordinates were followed from the transition state to the reactant and the product using the intrinsic reaction coordinate (IRC)[31,32] technique to further confirm the transition state obtained. To obtain accurate energies for reaction profiles, single point (sp) energies were calculated at the B3LYP/(LanL2DZ+6-311++G(2d,2p)) level of theory on the optimized structures. Solvent effects were accounted for by means of single point calculations on all stationary structures with isoelectric focusing polarized continuum model (IEF-PCM)[33–35]. The relative dielectric constant of water (ε_{water}=78.39) was used to approximate the bulk effects of solvation.

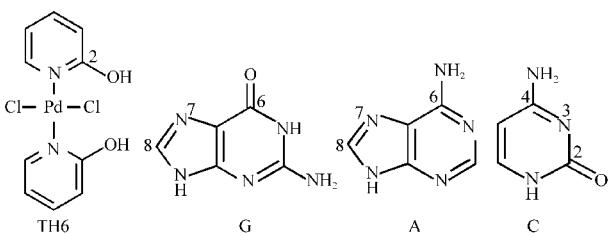

Fig.1 The labeling of TH6, guanine (G), adenine (A), and cytosine (C)

2 Results and discussion

2.1 Monofunctional reactions

As mentioned previously, Pd(II) complexes interaction with DNA bases have the similar mechanism as platinum (II) complexes: the N7 of guanine is the main target[36–38]. In monofunctional reactions chloroaqua and diaqua complexes of TH6 were considered as reactants to interact with guanine.

2.1.1 Chloroaqua complex acting as reactant

Fig.2 shows that in reactant complex the N7 and the O═C of guanine are hydrogen-bonded to the water ligand and one hydroxyl on the pyridine-based ligand, respectively.

Transition state is characterized by one imaginary frequency with 81.2i cm^{-1} and displays a strong hydrogen bond between the C═O of guanine and the leaving water. The distance between Pd and N7 of guanine is 0.268 nm. Fig.3(a) shows that the activation free energy of monoaquated TH6 binding to guanine is 52.8 kJ·mol^{-1} in aqueous solution, which is lower than that of cisplatin binding to guanine (102.9 kJ·mol^{-1})[13].

In product complex, the leaving water bridges a hydrogen bond between the C═O of guanine and one hydroxyl on the pyridine-based ligand (Fig.2). Reaction free energy of chloroaqua complex binding to guanine is –4.6 kJ·mol^{-1} in aqueous solution.

2.1.2 Diaqua complex acting as reactant

The hydrogen-bond patterns in the diaqua complex display a large similarity with the chloroaqua case. For reactant complex, the N7 and C═O of guanine are hydrogen-bonded to the water and 2-hydroxyl, respectively (Fig.4).

In transition state, the C═O···H—O···H_2O hydrogen bond

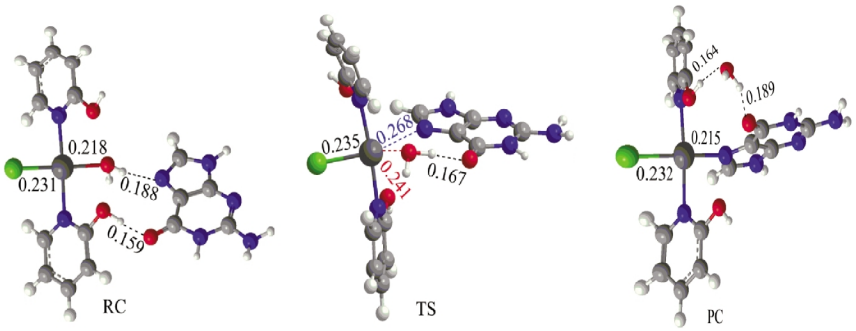

Fig.2 Stationary structures of reactant complex (RC), transition state (TS), and product complex (PC) of chloroaqua complex reacting with guanine (distance in nm)

network is formed among guanine, one hydroxyl on the pyridine-based ligand, and the water ligand as illustrated in Fig.4. In addition, a hydrogen bond formed between the leaving water and the other hydroxyl. The distance between the Pd and the N7 of guanine is 0.255 nm. Without expectation one imaginary frequency for the transition state is found with 90.6i cm^{-1}. The activation free energy of diaqua complex binding to guanine is 65.3 $kJ \cdot mol^{-1}$ in aqueous solution (Fig.3(b)), which is significantly lower than those of cisplatin (81.6 $kJ \cdot mol^{-1}$ [20]) and antitumor-active *trans* platinum complex (91.6 $kJ \cdot mol^{-1}$ [18]).

For product complex, the intramolecular hydrogen bond is formed between the C═O of guanine and one hydroxyl on the pyridine-based ligand (Fig.4). The hydrogen bond between the guanine and ligand is key for inducing structure distortions of DNA double helix as known from platinum-based drugs[39-41]. In addition, the retaining water ligand donates hydrogen to form hydrogen bond with the other hydroxyl and the leaving water is hydrogen-bonded to the H8 of guanine. Free energy of reaction for diaqua complex binding to guanine is –10.9 $kJ \cdot mol^{-1}$.

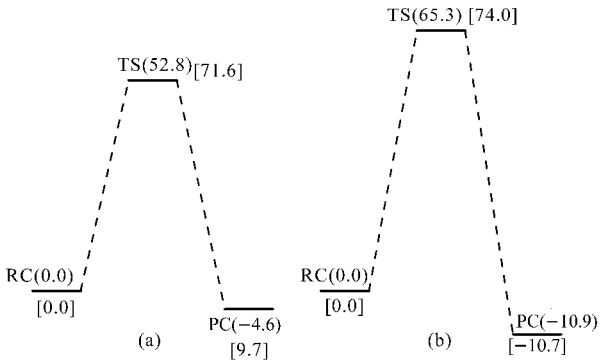

Fig.3 Computed reaction free energy (unit in $kJ \cdot mol^{-1}$) profiles for the chloroaqua (a) and diaqua (b) complexes binding to guanine

Gas phase and solution phase energies are given in square and round brackets, respectively.

Comparing chloroaqua complexes with diaqua complexes, the activation free energy of chloroaqua complex binding to guanine is lower than that of diaqua complex, which is due to Cl^- having stronger *trans* effect than water[42]. Due to high intrinsic reactivity of Pd[43], the activation free energies for TH6 binding to guanine are significant lower than those of platinum complexes.

2.2 Bifunctional reactions

According to the result in last section, we predict that the reaction rates of monofunctional binding to guanine for TH6 will be larger than that of platinum-based agents. However, it is still dubitable whether the monofunctional adducts of guanine of TH6 (*trans*-Pd[G(H_2O)]$^{2+}$) could further interact with DNA bases affording bifunctional adducts. Earlier speculation states that the great steric hindrance provided by two planar amine ligands will hinder formation of bifunctional adducts[10]. In the following sections we explored the feasibility of *trans*-Pd[G(H_2O)]$^{2+}$ interaction with guanine, adenine, and cytosine, respectively, to form bifunctional adducts. The N7 of purine base and N3 of cytosine[38] are main targets. As described previously, there are mainly two

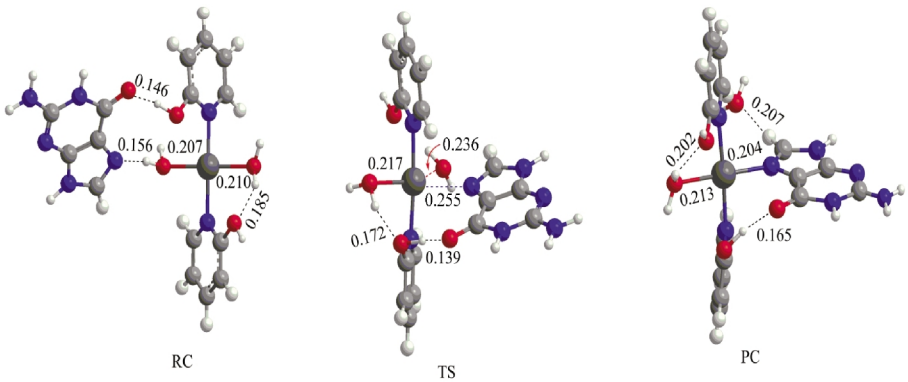

Fig.4 Stationary structures of reactant complex (RC), transition state (TS), and product complex (PC) of diaqua complex reacting with guanine (distance in nm)

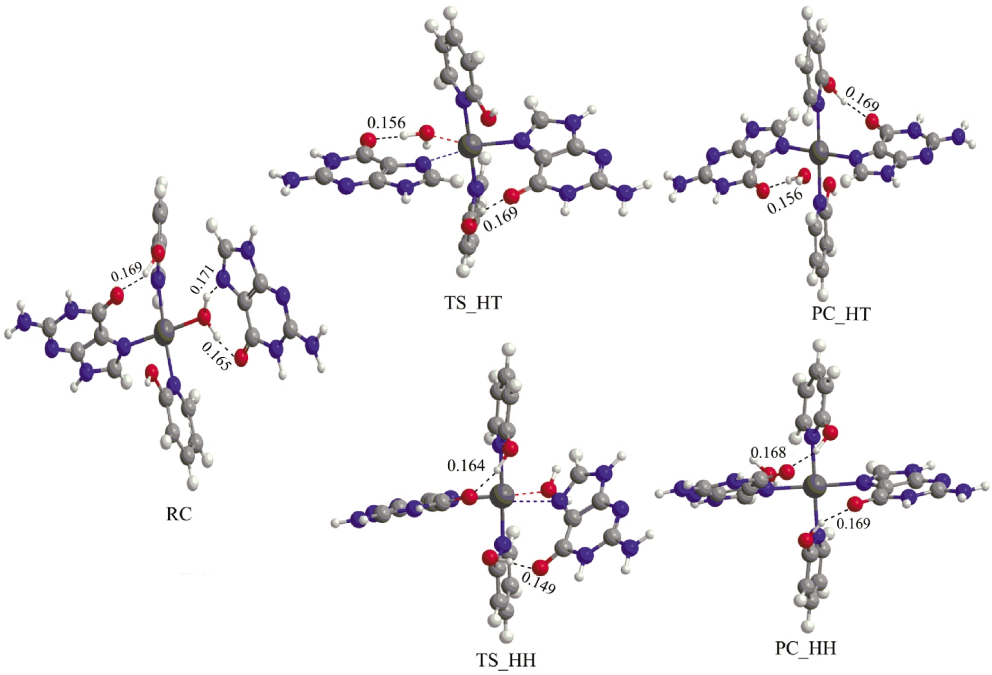

Fig.5 Stationary structures of reactant complex (RC), transition states (TS), and product complexes (PC) for monofunctional adducts of guanine bifunctional binding to guanine (distance in nm)

types of bifunctional products, PC_HH and PC_HT, and the corresponding transition states are denoted as TS_HH and TS_HT.

2.2.1 Reactions affording *trans*-Pd[G]$_2^{2+}$ bifunctional product

In reactant complex, the water ligand forms hydrogen bonds with the N7 and the C═O of the entering guanine. In addition, the intramolecular hydrogen bond is formed between the C═O of the other guanine and one hydroxyl on the pyridine-based ligand (HO—C2) as shown in Fig.5.

For transition states, TS_HH and TS_HT are characterized by one imaginary frequency with 93.6i and 85.5i cm^{-1}, respectively. The C═O of the entering guanine forms a hydrogen bond with hydroxyl on the ligand in TS_HH but in TS_HT the C═O of the entering guanine forms a hydrogen bond with the leaving water. The hydrogen bonds between the C═O of the other guanine and hydroxyl of the ligand are formed in both isomers (Fig.5). The distance between N7 of entering guanine and Pd in TS_HH is 0.272 nm, while it is 0.254 nm in TS_HT. The longer distance between Pd and N7 in TS_HH can be ascribed to greater steric repulsion between the entering guanine and palladium moiety. Fig.6 shows that TS_HT is 24.4 kJ·mol^{-1} preferred in energy over TS_HH in gas phase. Adding solvation free energy increases the energy difference further to give a preference of TS_HT over TS_HH by 28.9 kJ·mol^{-1}. The activation free energies for HT and HH paths are 46.0 and 74.9 kJ·mol^{-1} in aqueous solution, respectively (Fig.6). Our calculations demonstrate that the activation free energies of monofunctional adduct of guanine of TH6 binding to guanine are lower than that of cisplatin (88.7 kJ·mol^{-1} [20]) and antitumor-active *trans* platinum complex (99.2 kJ·mol^{-1}[18]). This suggests that the large planar amine ligands in TH6 will not hinder formation of *trans*-Pd[G]$_2^{2+}$ bifunctional adducts.

Two isomers of adducts are generated for TH6. The leaving water bridges a hydrogen bond between the C═O of one guanine and the H8 of the other guanine in PC_HT. In PC_HH, the C═O···HO—C2 and the H_2O···H8 hydrogen bonds are formed (Fig.5). The hydrogen bond between the C═O of the other guanine and hydroxyl is formed in both PC_HH and PC_HT and the hydrogen bond between ligands and DNA bases is important for antitumor activity as known from platinum-based antitumor agents[39-41]. PC_HT is 15.1 kJ·mol^{-1} more favorable in energy than PC_HH in aqueous solution, which is likely due to larger steric factor in PC_HH. Free energies of reactions affording PC_HT and PC_HH in aqueous solution are −34.3 and −19.2 kJ·mol^{-1} (Fig.6), respectively.

2.2.2 Reactions affording *trans*-Pd[GA]$^{2+}$ bifunctional products

In this section, we investigate reactions of monofunctional

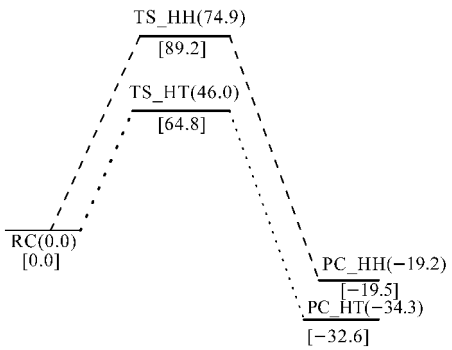

Fig.6 Computed reaction free energy (unit in kJ·mol^{-1}) profiles for the monofunctional adducts of guanine of TH6 binding to guanine

Gas phase and solution phase energies are given in square and round brackets, respectively.

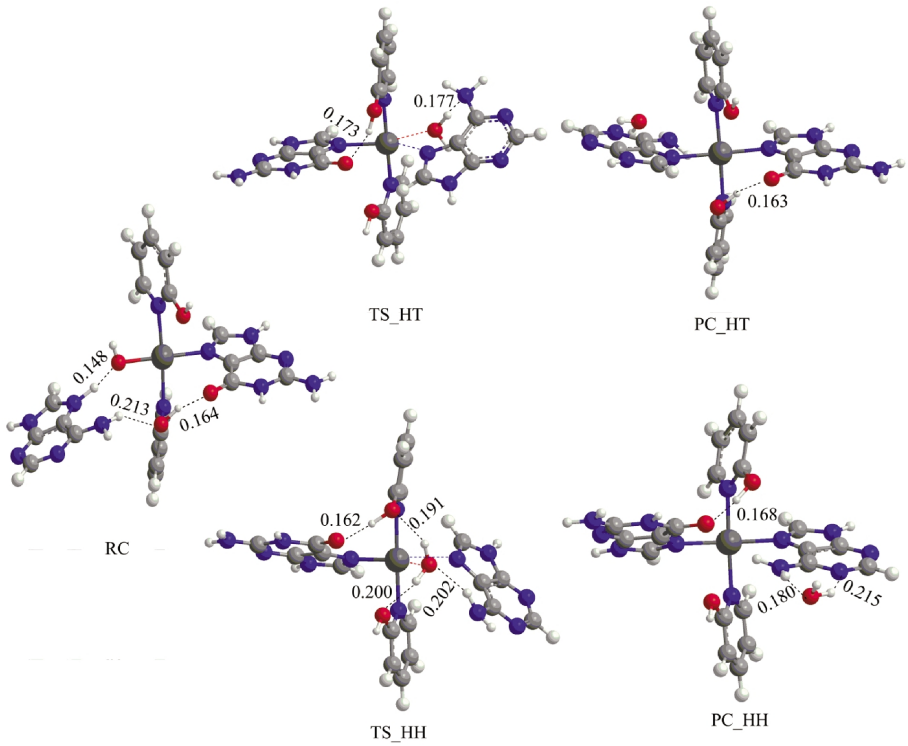

Fig.7 Stationary structures of reactant complex (RC), transition states (TS), and product complexes (PC) for monofunctional adducts of guanine bifunctional binding to adenine (distance in nm)

adduct of guanine binding to adenine affording *trans*-Pd[GA]$^{2+}$ bifunctional adducts. Fig.7 shows that proton of the water ligand transfers to the N7 of adenine and the C—NH_2···O—H···O=C hydrogen bond network formed among the adenine, hydroxyl on the 2-hydroxypyridine ligand, and guanine in reactant complex.

Two transition states, TS_HH and TS_HT, are located. TS_HT displays one imaginary frequency with 94.8i cm^{-1} and 48.6i cm^{-1} for TS_HH. In TS_HT, the amino group at the C6 of adenine act as hydrogen bond acceptor to form hydrogen bond with the leaving water and the hydroxyl on the pyridine-based ligand is hydrogen-bonded to the O=C of the guanine (Fig.7). In TS_HH the C—NH_2···OH_2···O=C hydrogen bond network is observed among the entering adenine, the leaving water and the guanine as illustrate in Fig.7. The distances between the N7 of attacking adenine and Pd are 0.272 and 0.254 nm for TS_HH and TS_HT, respectively. The 0.018 nm longer in the distance between Pd and N7 is likely due to larger steric repulsion in TS_HH. As shown in Fig.8, TS_HT is 9.0 kJ·mol^{-1} lower in energy than TS_HH. Adding solvation free energy decreases this energy difference slightly to give a preference for TS_HT over TS_HH by 2.9 kJ·mol^{-1}. The activation free energies of HT and HH in aqueous solution are 63.6 and 66.5 kJ·mol^{-1} (Fig.8), respectively. Our calculations reveal that activation free energies of monofunctional adducts of guanine of TH6 binding to adenine are lower than that of cisplatin (88.3 kJ·mol^{-1}[19]) and our recent study on antitumor-active *trans* platinum complex (72.0 kJ·mol^{-1} [18])in aqueous solution. This indicates that reactions affording *trans*-Pd[GA]$^{2+}$ adducts are possible.

In products, the C2—OH···O=C and C—NH_2···OH_2···N1 hydrogen bonds are observed in both PC_HT and PC_HH (Fig. 7). The hydrogen bond formed between 2-hydroxypyridine and DNA bases plays an important role in antitumor activity. Free energies of reactions affording PC_HH and PC_HT in aqueous solution are –25.9 and –11.3 kJ·mol^{-1}, respectively.

2.2.3 Reactions affording *trans*-Pd[GC]$^{2+}$ bifunctional product

The N3 of the cytosine is one of the targets of palladium (II) complex, and we explored *trans*-Pd[G(H_2O)]$^{2+}$ binding to cytosine.

In reactant complex, the N3 and C=O of cytosine are hydrogen-bonded to the water ligand and one hydroxyl on the pyridine-

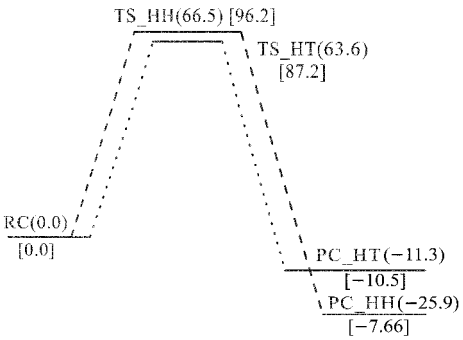

Fig.8 Computed reaction free energy (unit in kJ·mol^{-1}) profiles for the monofunctional adducts of guanine of TH6 binding to adenine

Gas phase and solution phase energies are given in square and round brackets, respectively.

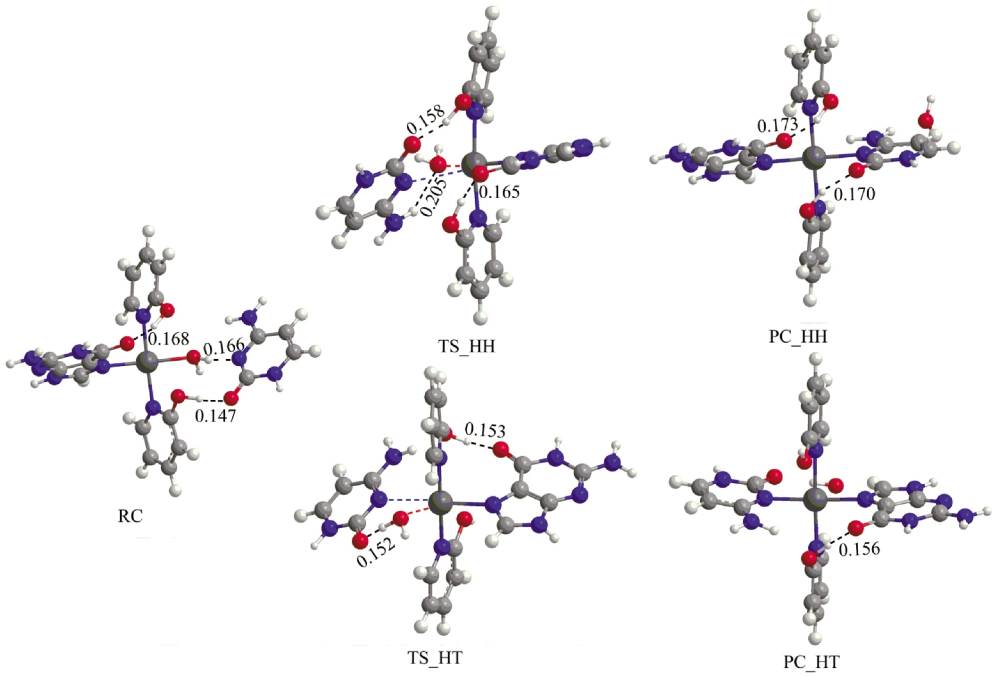

Fig.9 Stationary structures of reactant complex (RC), transition states (TS), and product complexes (PC) for monofunctional adducts of guanine of TH6 bifunctional binding to cytosine (distance in nm)

based ligand, respectively (Fig.9). In addition, an intramolecular hydrogen bond is formed between the C═O of guanine and 2-hydroxypyridine ligand.

Transition states obtained shows one imaginary frequency with 103.4i cm^{-1} for TS_HT and 135.7i cm^{-1} for TS_HH. In TS_HH, the leaving water bridges a hydrogen bond between the N3 and the NH_2—C4 of the entering cytosine. The C═O of the cytosine and the C═O of the guanine form hydrogen bonds with two hydroxyls at 2-hydroxypyridine ligands, respectively (Fig. 9). In TS_HT, the C═O···H_2O hydrogen bond is observed between the entering cytosine and the leaving water and the hydroxyl on the pyridine-based ligand bridges the hydrogen bond between the C4—NH_2 of the entering cytosine and O═C of guanine: C4—NH_2···O—H···O═C6. Our calculations reveal that the energy difference between the TS_HH and TS_HT is −0.1 kJ·mol^{-1} in solution phase. Fig.10 shows that the activation free energies of HT and HH paths in aqueous solution are 74.8 and 74.7 kJ·mol^{-1}, respectively. Our calculated activation barriers for monofunctional adducts of guanine binding to cytosine are lower than that of recent study on cisplatin[13,19,20] and our study on antitumor-active *trans* platinum complex[18] interaction with purine base to afford $Pt[G]_2^{2+}$ and $Pt[GA]^{2+}$. This indicates that reactions affording *trans*-$Pd[GC]_2^{2+}$ are possible.

In the PC_HH, the C═O of the cytosine and the C═O of the guanine form hydrogen bonds to two hydroxyls at 2-hydroxypyridine ligands, respectively and the C4—NH_2 of the cytosine is hydrogen bonded to the water. In the PC_HT, one hydroxyl bridges hydrogen bond between the C4—NH_2 of cytosine and the O═C of the guanine and the leaving water bridges a hydrogen bond between the C—O of cytosine and H8 of guanine (Fig. 9). Our calculations reveal that PC_HT is 7.1 kJ·mol^{-1} preferred in free energy over PC_HH in solution phase. Fig.10 shows that free energies of reactions affording PC_HH and PC_HT in aqueous solution are −18.4 and −25.5 kJ·mol^{-1}, respectively.

Our calculations demonstrate that monofunctional adducts of guanine of TH6 binding to purine bases and cytosine show lower activation free energies comparing with those of platinum-based drugs. This suggests that the bifunctional binding to DNA bases is possible for TH6 and the large planar amine ligands in TH6 will not hinder formation of bifunctional adducts with DNA base and even the rate for monofunctional adducts conversion into bifunctional adducts will be larger than that of platinum-based agents. The reaction affording *trans*-$Pd[G]_2^{2+}$ *via* HT path shows the lowest activation free energy. This suggests that the bifunctional reactions affording *trans*-$Pd[G]_2^{2+}$ is larger than

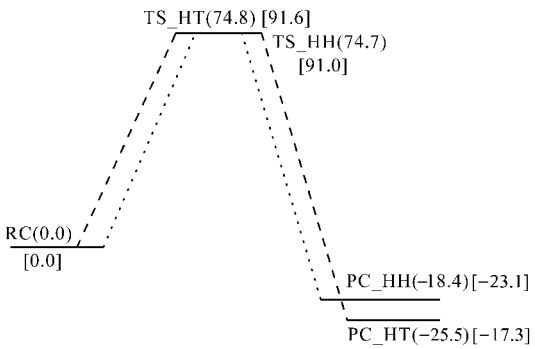

Fig.10 Computed reaction free energy (unit in kJ·mol^{-1}) profiles for the monofunctional adducts of guanine of TH6 binding to cytosine

Gas phase and solution phase energies are given in square and round brackets, respectively.

those for *trans*-Pd[GC]$^{2+}$ and *trans*-Pd[GA]$^{2+}$. The preference of bifunctional binding to guanine over adenine and cytosine for TH6 is similar to the platinum-based antitumor drug interaction with DNA bases.

3 Conclusions

We have explored of palladium (II) complex with large planar amine ligands monofunctional binding to guanine and then bifunctional binding to guanine, adenine, and cytosine, respectively, by quantum chemical method. Our calculation clearly illustrates that the large planar amine ligands in TH6 will not hinder formation of bifunctional adducts with DNA bases, and even the rate for monofunctional adducts conversion into bifunctional adducts will be larger than that of platinum based agents. For bifunctional binding, the kinetic preference for binding to guanine over adenine and cytosine is observed. We also find strong hydrogen bonding interactions between 2-hydroxypyridine ligands and DNA bases. The strong hydrogen bonds are important for inducing structure distortions of the DNA double helix and antitumor activity from classical structure-activity relationship (SAR) rules based on platinum based drugs.

References

1 Jung, Y.; Lippard, S. J. *Chem. Rev.*, **2007, 107**: 1387

2 Fuertes, M. A.; Alonso, C.; Perez, J. M. *Chem. Rev.*, **2003, 103**: 645

3 Mohamed, M. M. A.; Shoukry, M. M. *Polyhedron*, **2001, 20**: 343

4 Barnham, K. J.; Bauer, C. J.; Djuran, M. I.; Mazid, M. A.; Rau, T.; Sadler, P. J. *Inorg Chem.*, **1995, 34**: 2826

5 Kuduk-Jaworska, J.; Puszko, A.; Kubiak, M.; Pelczynska, M. *J. Inorg. Biochem.*, **2004, 98**: 1447

6 Budzisz, E.; Krajewska, U.; Rozalski, M.; Szulawska, A.; Czyz, M.; Nawrot, B. *Eur. J. Pharmacol.*, **2004, 502**: 59

7 Mock, C.; Puscasu, I.; Rauterkus, M. J.; Tallen, G.; Wolff, J. E. A.; Krebs, B. *Inorg. Chim. Acta*, **2001, 319**: 109

8 Ma, Y.; Day, C. S.; Bierbach, U. *J. Inorg. Biochem.*, **2005, 99**: 2013

9 Navarro, M.; Pena, N. P.; Colmenares, I.; Gonzalez, T.; Arsenak, M.; Taylor, P. *J. Inorg. Biochem.*, **2006, 100**: 152

10 Huq, F.; Tayyem, H.; Beale, P.; Yu, J. Q. *J. Inorg. Biochem.*, **2007, 101**: 30

11 Keter, F.; Kanyanda, S.; Lyantagaye, S.; Darkwa, J.; Rees, D.; Meyer, M. *Cancer Chemother. Pharmacol.*, **2008, 63**: 127

12 Gao, E. J.; Sun, Y. G.; Liu, Q. T.; Duan, L. Y. *J. Coord. Chem.*, **2006, 59**: 1295

13 Baik, M. H.; Friesner, R. A.; Lippard, S. J. *J. Am. Chem. Soc.*, **2003, 125**: 14082

14 Fichtinger-Schepman, A. M. J.; van Oosterom, A. T.; Lohman, P. H. M.; Berends, F. *Cancer Res.*, **1987, 47**: 3000

15 Eastman, A. *Biochemistry*, **1986, 25**: 3912

16 Fregona, D.; Giovagnini, L.; Ronconi, L.; Marzano, C.; Trevisan, A.; Sitran, S.; Biondi, B.; Bordin, F. *J. Inorg. Biochem.*, **2003, 93**: 181

17 Akdi, K.; Vilaplana, R. A.; Kamah, S.; Gonzalez-Vilchez, F. *J. Inorg. Biochem.*, **2005, 99**: 1360

18 Zhou, L. *J. Phys. Chem. B*, **2009, 113**: 2110

19 Mantri, Y.; Lippard, S. J.; Baik, M. H. *J. Am. Chem. Soc.*, **2007, 129**: 5023

20 Raber, J.; Zhu, C.; Eriksson, L. A. *J. Phys. Chem. B*, **2005, 109**: 11006

21 He, Q.; Zhou, L. X. *Acta Phys. -Chim. Sin.*, **2005, 21**: 846 [和 芹, 周立新. 物理化学学报, **2005, 21**: 846]

22 Deubel, D. V. *J. Am. Chem. Soc.*, **2004, 126**: 5999

23 Deubel, D. V. *J. Am. Chem. Soc.*, **2002, 124**: 5834

24 Zimmermann, T.; Chval, Z.; Burda, J. V. *J. Phys. Chem. B*, **2009, 113**: 3139

25 Becke, A. D. *J. Chem. Phys.*, **1993, 98**: 5648

26 Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B*, **1988, 37**: 785

27 Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; *et al*. Gaussian 03, Revision D.01. Wallingford CT: Gaussian, Inc., 2004

28 Wadt, W. R.; Hay, P. J. *J. Chem. Phys.*, **1985, 82**: 284

29 Hay, P. J.; Wadt, W. R. *J. Chem. Phys.*, **1985, 82**: 299

30 Hay, P. J.; Wadt, W. R. *J. Chem. Phys.*, **1985, 82**: 270

31 Gonzalez, C.; Schlegel, H. B. *J. Phy. Chem.*, **1990, 94**: 5523

32 Carlos, G.; Schlegel, H. B. *J. Chem. Phys.*, **1989, 90**: 2154

33 Tomasi, J.; Mennucci, B.; Cances, E. *J. Mol. Struct. -Theochem,* **1999, 464**: 211

34 Mennucci, B.; Tomasi, J. *J. Chem. Phys.*, **1997, 106**: 5151

35 Mennucci, B.; Cances, E.; Tomasi, J. *J. Phys. Chem. B*, **1997, 101**: 10506

36 Riera, X.; Moreno, V.; Freisinger, E.; Lippert, B. *Inorg. Chim. Acta*, **2002, 339**: 253

37 Akdi, K.; Vilaplana, R. A.; Kamah, S.; Navarro, J. A. R.; Salas, J. M.; Gonzalez-Vilchez, F. *J. Inorg. Biochem.*, **2002, 90**: 51

38 Nikolis, N.; Methenitis, C.; Pneumatikakis, G. *J. Inorg. Biochem.*, **2003, 95**: 177

39 Reedijk, J. *Inorg. Chim. Acta*, **1992, 198–200**: 873

40 Cleare, M. J.; Hoeschele, J. D. *Bioinorg. Chem.*, **1973, 2**: 187

41 Cleare, M. J.; Hoeschele, J. D. *Platinum Met. Rev.*, **1973, 17**: 2

42 Chval, Z.; Sip, M.; Burda, J. V. *J. Comput. Chem.*, **2008, 29**: 2370

43 Burda, J. V.; Zeizinger, M.; Leszczynski, J. *J. Chem. Phys.*, **2004, 120**: 1253