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Metal-mediated thymine base pair complexes: A DFT study

Ayhan ÜNGÖRDÜ [1], Nurten TEZER

Cumhuriyet University, Science Faculty, Chemistry Department, 58140 Sivas / Turkey

Abstract: The most stable of thymine-metal-thymine complexes and their geometries were determined. Method was used density functional theory, B3LYP. The calculations of systems containing C, H, N, O were described by the standard 6–311++G(d,p) basis set and LANL2DZ basis set were used for transition metals. Egap energy values of complexes were calculated by Chemissian program. Conductivity of metal-mediated thymine base pair complexes were predicted. In nanoworld, this study is expected to be shown the way for future practical applications.

Keywords: *metal-DNA; conductivity; nanowires; DFT calculations.*

1. Introduction

Nucleic acids, linked chains purine (adenine and guanine) and pyrimidine (uracil, thymine and cytosine) bases carries the genetic information in living systems. Recently, there have been many studies to explain the properties of the nucleic acids in nonbiological contexts. Some properties of nucleic acids enable them to be used to produce the nanostructures (nanomaterials, nanowires…) [1]. One of the properties of the nucleic acids is to form metal-DNAs. Metal-DNAs may be obtained by treatment with double-stranded DNA of the metal cation [2]. Alkali (or rare-earth) cations form only electrostatic interactions with the nucleobases [3,4], but transition metal cations are expected to interact with the nucleobases also by chemical bonding [5-10]. Additionally, transition metals have many functions in the nanoworld. Due to the unique physical and chemical properties related to electronic conductivity of metal ions, they are involved in nucleic acids to form metal-mediated DNA bases [11]. DNA-based nanostructures can be formed in this way. DNA-based nanostructures attract attention because of their unique electrical, optical biological applications. The production of metal-DNA provides substantial benefits for their potential application as nanomagnets [12,13], as nanowires or as catalysts in chemical reactions.

Recently, metal-DNA have attracted much interest for the possibility of using such molecules as building blocks for electronic nano-devices [14-17]. If natural DNA would be a superior conductor for electrons and functional building blocks such as molecular transistors could be incorporated into DNA strands by chemical synthesis, it would be possible to construct the first generation of electronic circuits today (Fig. 1).

1.1. Metal-mediated thymine base pairs

The simplest pyrimidine base is thymine. It has become an important subject of theoretical or experimental work due to the biochemical importance [18,19]. It has been reported that natural thymine bases form metal-DNA. Two thymine (T–T) bases selectively capture mercury(II) cations and T-Hg-T complex forms. This complex occurs easily with mercury(II) cations [20-23]. T-Hg-T complex is

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[1] Corresponding Author

e-mail: aungordu@cumhuriyet.edu.tr

formed by displacement of metal-base bond with hydrogen bond in natural DNA and they are also mismatched (Fig. 2) [24].

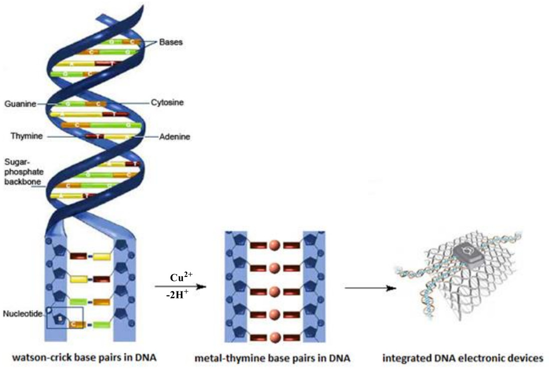


Fig. 1. The use of metal-DNA as conductive wires in nanotechnology.

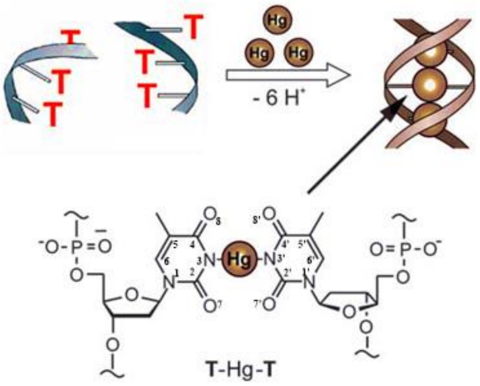


Fig. 2. Formation of T-Hg-T complex from upon addition of Hg^{2+} ions [20].

Studies from a number of groups have shown that mercury(II) ion binds to the nitrogen atoms between T–T mismatches (Fig. 2). One of them is Ono group. This group has found strong evidence for the structure of T–Hg–T by N15-NMR spectroscopy. ESI-MS spectroscopy has determined that up to five mercury(II) ions can stack between T-T bases (similarly to Fig. 1) [20,21].

After many studies in this area, it is known that the transition metal ion binding sites on the thymine consists primarily of the deprotonated nitrogen atoms (N3) and the oxygen positions (O7 or O8), depending on the coordinating metal [25-27]. Therefore, deprotonated thymine can be considered as bidentate ligand. Two main coordination geometries are expected for two bidentate ligands around a central metal ion: square planar and tetrahedral [24].

At high pH conditions, divalent metal cations (Zn^{2+}, Ni^{2+} and Co^{2+}) were reported by the Lee group to form complexes with unmodified DNA [28]. Upon adding these metal ions to DNA at pH 8.5, a pH decreases and NMR results were consistent with replacement of the imino proton (at N3) in each base pair of the duplex by a metal ion. Such metal–DNA complexes can be more conductive than DNA, with potential for the development of molecular wires and useful nanotechnological applications [28-30]. However, the exact structure and the electronic properties of metal-DNA are still controversial [31,32]. For instance, AFM study of metal-DNA duplexes showed that they have a very condensed structure compared to DNA duplexes that has yet to be explained [31].

The main goal of this work is to unravel conductivity of metal-mediated thymine base pairs for some divalent transition metal ions. We present and discuss the results of a DFT study of several metal-mediated T–M^{n+}–T complexes (M = Hg, Cd, Zn, Cu, Ni, Pd, Pt and n = 2) in the gas phase. We find that all of the examined metal species are capable of binding Thymine–Thymine (T-T) base pairs in the ratio 1:2, and the resulting T–M^{n+}–T base pairs have a low band gap. Using band gap, we determine the metal-DNA complex that creates the suitable conductor wire. These complexes are considered to be useful for nanotechnological applications.

2. Computational Details

Metal-mediated thymine base pair complexes were investigated by means of density functional theory (DFT) calculations. Because previous theoretical calculations shown that the B3LYP approach was cost-effective for studying transition metal-ligand systems [33]. The calculations of systems containing C, H, N, O were described by the standard 6–311++G(d,p) basis set [34]. For transition metals (Hg, Cd, Zn, Cu, Ni, Pd and Pt), LANL2DZ basis set was used [35] and Hg, Cd, Zn, Cu, Ni, Pd and Pt were described by the effective core potential (ECP) of Wadt and Hay pseudopotential [36,35b] with a doublet–ζ valence using the LANL2DZ. All of the systems were optimized at the B3LYP method. In all cases, the steady–state nature of the optimized metal-mediated thymine base pair complexes were confirmed by calculating the corresponding frequencies at the same computational level. For the optimized geometries, the correlation energies were calculated by B3LYP density functional theory. The calculations were performed by using the GAUSSIAN 09-Revision D.01 package program [36]. The input files of mentioned complex were prepared with GaussView 5.0.8 program [37]. Closed-shell calculations were performed using the restricted formalism and open-shell calculations were performed using the unrestricted formalism (for Cu^{2+}). The energy difference (Egap) between HOMO and LUMO were calculated by using the Chemissian, version 4.43 demo program [38] (created in Chemissian based on Gaussian 09 calculations). The energy gaps were given as follows.

$$Egap = E_{LUMO} - E_{HOMO}$$

The band theory is related to molecular orbital theory [39]. In molecular orbital theory, while the highest occupied molecular orbital is called HOMO, the lowest unoccupied molecular orbital is called LUMO. The valence band (VB) represents HOMO and the conduction band (CB) represents LUMO [40]. The gap between the HOMO and LUMO level is called band gap or energy gap (Egap). The conductivity of metal-DNA can be examined by energy gap (Fig. 3).

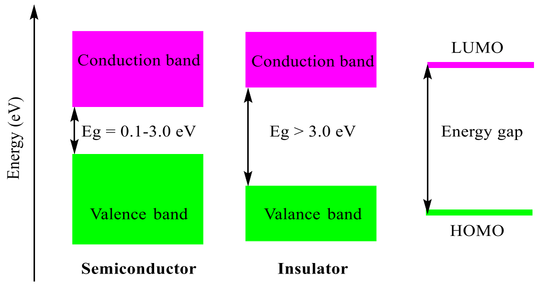
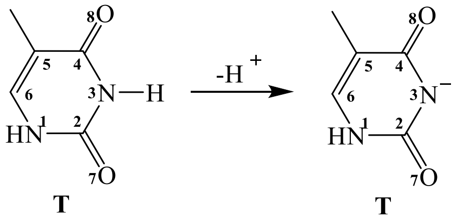


Fig. 3. The correlation between energy band diagram and HOMO-LUMO [39].

3. Results and Discussion

Thymine have an acidic imine proton. Therefore, imine proton is lost in the basic medium. Deprotonated thymine is formed as following:



Metal-mediated thymine base pair complex can occur that metal cation react with deprotonated thymine anion. Formation of this reaction can show as in Fig. 4. As shown in the above reaction, metal cation (M^{2+}) binds from the region of deprotonated thymine anion (T^{-}) where the electron density is very (red area). Possible binding structures of Cu-mediated thymine base pairs is represented as in Fig. 5.

For these structures, relative energy values are given in Table 2. Considering the relative energy values, it is seen that the most stable structure is III structure. This can be explained as follows: Electronegative N atom at 1 position 1 of deprotonated thymine, by inductive effect, decreases the electron density of N3-O7 region of ligand. On the other hand, this cannot be said for N3-O8 region of ligand. Therefore, electron density of N3-O8 region is more than that of N3-O7 region. When metal binds from this region, the most stable complexes form. This is true for all complexes.

We have performed the calculations of ΔG and the results, at 298 K are reported in Table 3. We here define the complex formation energy by following formula:

$$\Delta G_{form.} = G_{T-M-T} - (2G_{T^-} + G_{M^{2+}})$$

Table 2. Relative energies ($kcal.mol^{-1}$) of three possible Cu-mediated thymine base pair complexes

Method	I	II	III
B3LYP/G-311++(d,p)-LANL2DZ (Cu)	0	-1,23	-6,28

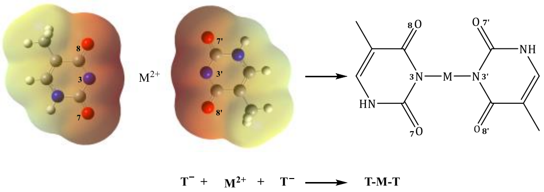


Fig. 4. The reaction pathway for metal mediated thymine base pair complexes

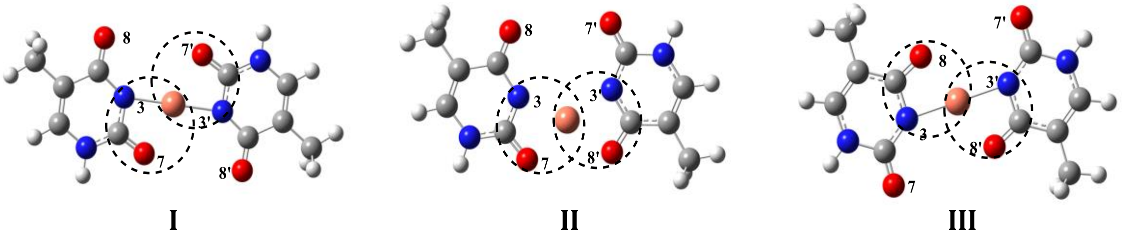


Fig. 5. Three possible binding structure for Cu-mediated thymine base pairs complex

It is seen from Table 3 that the studied complexes can be synthesized with reaction metal cation (M^{2+}) and deprotonated thymine anion (T^{-}) if required conditions provide (such as pH). Also, it is found that the especially planar complexes are more stable (~100 kcal/mol) than the non-planar complexes. Table 3 represents the complex formation energy, ΔG_{form}, which ranges from -525 kcal mol^{-1} (for Cd^{2+}) to -679 kcal mol^{-1} (for Pt^{2+}). The T-Pt-T is the most stable complex among all metal complexes.

A different look at the role of the metal moiety in the electronic structure of metallated base pairs can be given by inspecting the electron energy levels and the HOMO-LUMO gaps. In all of the computed T-M-T pairs the Egap changes by depending on the complex coordination. The energy gap change is an important metal-induced effect in view of nanotechnology applications. M-DNA's conductivity mechanism by electronic means is not yet fully elucidated [42]. One of the theoretical approach to explain the electrical conductivity is the band theory. In this work, the electrical conductivity of the T-M-T complexes have also tried to explain the band theory. For this, the frontier orbital energy levels for the most stable structures of metal complexes are found and the energy gaps (Egap) are determined. Egap values are calculated using the difference HOMO-LUMO values. We can divide into double-electron (closed-shell) and single-electron (open-shell) systems of examined complex structures. Except Cu^{2+}, studied other metal cation systems are closed-shell.

Table 3. Complex formation energies of T-M-T complexes (at 298,15 K)

Metal type	**G(Thymine anion)/a.u.**	**G (Metal cation/a.u.**	**G (Complex)/a.u.**	**ΔG(Complex)/kcal mol^{-1}**
Hg(II)	-453,644	-41,811	-949,942	**-529**
Cd(II)	-453,644	-47,173	-955,297	**-525**
Zn(II)	-453,644	-64,642	-972,843	**-573**
Cu(II)	-453,644	-195,081	-1103,356	**-619**
Ni(II)	-453,644	-168,177	-1076,522	**-664**
Pd(II)	-453,644	-125,592	-1033,926	**-656**
Pt(II)	-453,644	-117,978	-1026,349	**-679**

Ha: Hartree and Method: B3LYP/G-311++(d,p)-LANL2DZ (Metal)

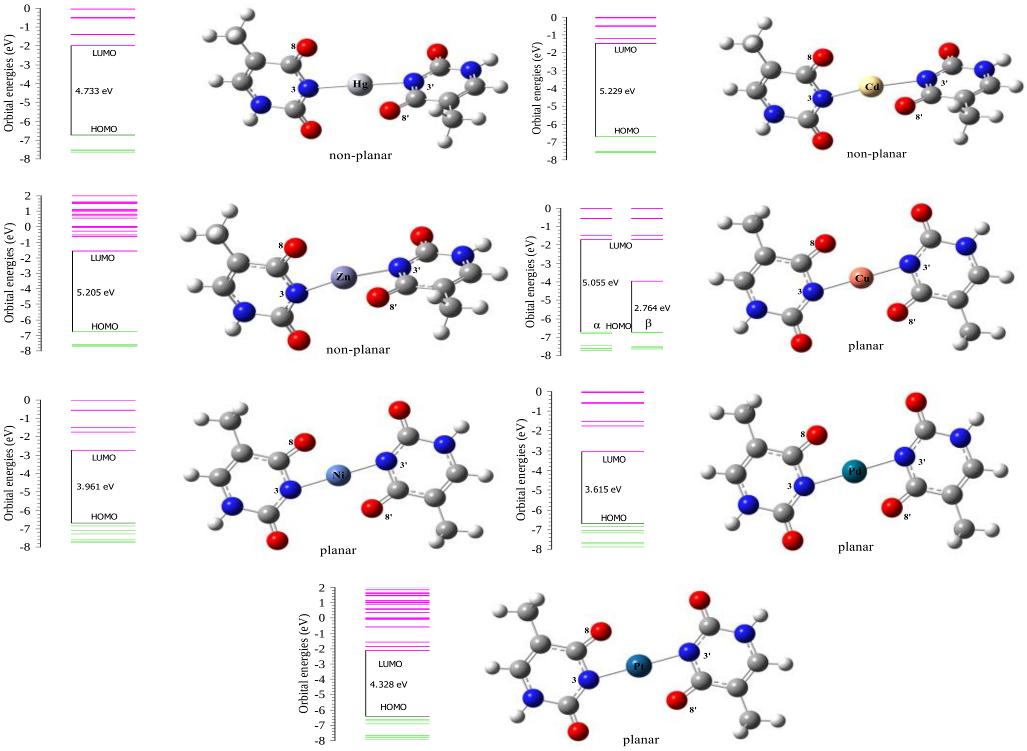
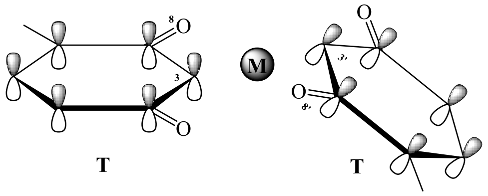


Fig. 6. Optimized metal-mediated thymine complexes and their HOMO-LUMO energy gaps. Atoms are shown in a ball and stick representation with standard colors. (Red=O; White=H; Blue=N; Cyan=C). In the orbital energies, green lines and pink lines represent HOMO (OMOs) and LUMO (UMOs) energy levels, respectively. Also, geometries are determined as planar or non-planar.

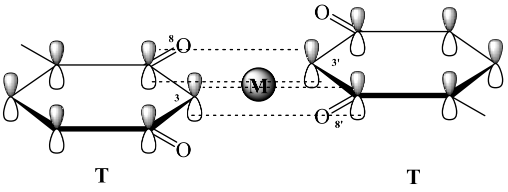
Orbital energy levels and Egap values (eV) for open- and closed-shell complexes are shown in Fig. 6. Referring from Fig. 6, the Egap values of complexes except Cu-complex can be seen that is over the insulation threshold 3 eV (as described in Fig. 3). All these metal complexes are included in the insulation class [39]. When the molecular orbital energy level of the Cu^{2+} (d^9 open-shell) complex is seen that the α-SOMO orbital (singly occupied molecular orbital) has lower energy than the β-HOMO orbital. The SOMO is similar the β-LUMO. Hence, it is clear that the lowest excitation occurs between β-HOMO and β-LUMO. In this system, β-HOMO–β-LUMO difference (2.764 eV) is taken into account for the Egap value. Looking at the other planar complexes, Egap values is seen that is over the 3 eV value. Only Cu-complex is included in the semiconductor class [39].

In many studies related to the conductivity, it is said the conductivity occurs via π-way [42-44]. Non-planar molecular orientation can be assumed in a geometrical manner such as described below:



Assumed π-π interaction
at non-planar complexes
(N atoms were hidden)

Referring to this figure, the conjugated π-system of the aromatic thymine ligand is difficult to overlap with the π-system of the ligand on the other side. In other words, π-π interaction is not possible. Therefore, it seems difficult to transmission of electricity through π system in these complexes. Our Egap values are consistent with this explanation. On the other hand, the molecular orientation of planar complexes can be assumed as follows:



Assumed π-π interaction at planar complexes (N atoms were hidden)

Referring to this orientation, the conjugated π-system of aromatic thymine is easy to overlap with the π-system of the other ligand. In these complexes, the transmission of electricity through π-system can be considered to be occur easily. Our Egap values support this idea. Egap values of planar complexes are lower than those of nonplanar complexes. Even so, Egap values of Ni, Pd ve Pt complexes are over 3 eV. However, these complexes are close to semiconductor class.

According to our calculations, for conductivity applications, most suitable complex is T-Cu-T complex. Among all investigated complexes, best conductor is complex obtained from Cu. This work is expected to lead to nanotechnological applications will be done in the future.

4. Conclusion

In summary, we theoretically design metal-mediated TT base pairs and explore their structure and energy level of the frontier orbitals with a DFT method. On the basis of the obtained results, the following conclusions can be drawn.

In all stable complexes, the metal cation is connected to the side of the deprotonated nitrogen atom (N3) and the oxygen atom at the 2-position of the pyrimidine base.

Our calculations have been carried out without any geometrical constraints. While T-M-T complexes formed from Hg, Cd and Zn metal cations are non-planar, the complexes formed from Cu, Ni, Pd and Pt are planar. It is observed that planarity increases the metal base distance decreases and the planar complexes are more stable than the nonplanar complexes. All the reactions are considerable exothermic and irreversible.

The Egap values of planar complexes are lower than those of nonplanar complexes. Among them, Cu-complex has the lowest Egap value. Thus, this complex is best conductor and it can be used for single nanowires.

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