

**ABANT İZZET BAYSAL UNIVERSITY
THE GRADUATE SCHOOL OF NATURAL AND APPLIED
SCIENCES**



**STUDIES OF THE REACTIONS OF SOME PYRIMIDINE
DERIVATIVES WITH SOME DNA NUCLEOBASES USING
QUANTUM MECHANICAL METHODS**

MASTER OF SCIENCE

GHIATH ASSAF

BOLU, JULY 2017

**ABANT İZZET BAYSAL UNIVERSITY
THE GRADUATE SCHOOL OF NATURAL AND APPLIED
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APPROVAL OF THE THESIS

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WITH SOME DNA NUCLEOBASES USING QUANTUM MECHANICAL
METHODS** submitted by **Ghiath ASSAF** in partial fulfillment of the requirements
for the degree of **MASTER OF SCIENCE** in **DEPARTMENT OF CHEMISTRY**,
ABANT IZZET BAYSAL UNIVERSITY by,

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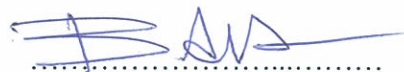
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اللَّهُمَّ اغْفِرْ لِي وَلِوَالِدَيَّ، رَبِّ اَرْحَمْهُمَا كَمَا رَبَّيْتَانِي صَغِيرًا

To the soul of my lovely, sweet and great mother

To my small and lovely family, Sawsan and Hadi

To my sweet family, my father

To my second family, my father and mother in law

To my lovely, sweet, great, and hurt Country

DECLARATION

I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

Ghiath ASSAF


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ABSTRACT

STUDIES OF THE REACTIONS OF SOME PYRIMIDINE DERIVATIVES WITH SOME DNA NUCLEOBASES USING QUANTUM MECHANICAL METHODS

MSC THESIS

GHIATH ASSAF

**ABANT IZZET BAYSAL UNIVERSITY GRADUATE SCHOOL OF
NATURAL AND APPLIED SCIENCES**

DEPARTMENT OF CHEMISTRY

(SUPERVISOR: PROF. DR. IZZET MORKAN)

BOLU, JULY 2017

Quantum mechanical calculations employing DFT/B3LYP method and (3-21G, 6-31G, 6-31G++dp and aug-cc-pVDZ) basis sets are conducted to investigate the properties of the pyrimidine and its derivatives with the DNA (Adenine, Guanine, Cytosine and Thymine). The bond lengths, bond angles, total energy, dipole moment and HOMO-LUNO were calculated and the results were very good comparing to the experimental data, and generally the biggest basis sets (6-31G++dp and aug-cc-pVDZ) were the most accurate. The pyrimidines have very important biological properties as chemotherapeutic agents, in addition to pyrimidines, cisplatin has a wide use as an anticancer agent. Hence, in this work novel complexes of platinum (II) with some DNA nucleobases (Adenine and Cytosine) were designed and optimized using DFT/B3LYP method and (3-21G, 6-31G, 6-31G++dp, and 6-311G) basis sets for (Carbon, Chlorine, Nitrogen, Oxygen and Hydrogen) atoms, for platinum atom two basis sets have been used, Stuttgart/Dresden (SDD) basis set is used for outer shell electrons, and Los Alamos National Laboratory 2 (LANL2) basis set (effective core potentials) is used for the core electrons. The calculations of frequency showed positive result for all complexes (no imaginary frequency) so all complexes are expected to be stable. Also, the bond lengths and bond angles of the complexes were compared to the experimental data of cisplatin and they have a good agreement.

Moreover, the dihedral values showed a good square planar geometry for Adenine complexes and some distortion in Cytosine complex. In the HOMO orbitals, electrons are localized mainly in the (Cl) leaving group of the complex, meanwhile in the LUMO orbitals, electrons are localized mainly over the ligand molecular part for all three complexes. Finally, the reaction pathway of synthesizing one of these three complexes has been studied and it is predicted to be non-spontaneous process with two steps, for the first step $\Delta G_1 = 4.79$ Kcal/Mol, and for second step $\Delta G_2 = 11.94$ Kcal/Mol.

KEYWORDS: DFT, Cisplatin, DNA, Adenine, Guanine, Cytosine, Thymine, Pyrimidine, Quantum mechanical methods, Platinum (II) complexes

ÖZET

KUANTUM MEKANIĞI METODLARI KULLANARAK, BAZI PİRİMİDİN TÜREVLERİNİN DNA NÜKLEO BAZLARIYLA TEPKİMELERİNİN İNCELENMESİ

YÜKSEK LİSANS TEZİ

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(TEZ DANIŞMANI: PROF. DR. İZZET MORKAN)

BOLU, TEMMUZ 2017

DFT/B3LYP metodu ve (3-21G, 6-31G, 6-31G++dp ve aug-cc-pVDZ) basis setleri, Pirimidin ve DNA Türevleri (Adenin, Guanin, Sitosin ve Timin) özelliklerini incelemek için kullanılmaktadır. Bağ uzunlukları, bağ açıları, toplam enerji, dipol moment ve HOMO-LUMO hesaplanmaktadır. Bu değerlerin deneysel sonuçlarla uyumlu olduğu ve genellikle en büyük basis setlerin (6-31G++dp ve aug-cc-pVDZ) en doğru olduğu anlaşılmıştır. Pirimidinler kemoterapik ajanlar olarak çok önemli bir biyolojik etkidir. Buna ek olarak, Cisplatin bir anti-kanser ajanı olarak en geniş kullanım alanına sahiptir. Dolayısıyla, bu çalışmada, Platinyum (II) ile bazı DNA Nükleobazlarının (Adenin ve Sitosin) yeni kompleksleri dizayn edilmiştir. DFT / B3LYP metodu ve atomlar (Karbon, Klor, Azot, Oksijen ve Hidrojen) için basis setleri (3-21G, 6-31G, 6-31G++dp ve aug-cc-pVDZ) kullanılarak tasarlanmış ve etkinleştirilmiştir. Platinyum atomu için iki basis set kullanılmıştır, Stuttgart/Dresden (SDD) basis seti dış kabuktaki elektronlar için kullanılmıştır, ve Los Alamos National Laboratory 2 (LANL2) basis seti de (etkin çekirdek potansiyeli) çekirdekteki elektronlar için kullanılmıştır. Frekans hesaplamaları tüm kompleksler için pozitif sonuç vermiştir (negatif frekans yok) ve böylece tüm komplekslerin kararlı olması beklenmektedir. Ayrıca, komplekslerin bağ uzunlukları ve bağ açıları Cisplatinin deneysel verisiyle karşılaştırılmıştır ve iyi sonuç alınmıştır. Üstelik dihedral değerleri, Adenin kompleksleri ve Sitosin kompleksindeki bazı bozulmalar için iyi bir kare

düzlem geometri göstermiştir. HOMO orbitallerinde, elektronlar başlıca kompleksin ayrılan grubunda (Klor) yer almaktadır. Aynı zamanda LUMO orbitallerinde, elektronlar bütün üç kompleks için ağırlıklı olarak ligand molekül kısmının üzerinde bulunmaktadır. Sonuç olarak, bu üç kompleksten birinin sentezinin reaksiyonu üzerine çalışmıştır ve iki basamakta kendiliğinden olmayan bir reaksiyon olması beklenmektedir, birinci basamak için $\Delta G_1=4.79$ kJ/mol ve ikinci basamak için $\Delta G_2=11.94$ kJ/mol olarak hesaplanmıştır.

ANAHTAR KELİMELEER: DFT, Cisplatin, DNA, Adenin, Guanin, Sitozin, Timin, Pirimidin, Kuantum Mekaniksel Metodlar, Platinum (II) Kompleksleri

TABLE OF CONTENTS

	<u>Page</u>
ABSTRACT	v
ÖZET	vii
TABLE OF CONTENTS	ix
LIST OF FIGURES	xi
LIST OF TABLES	xii
LIST OF ABBREVIATIONS AND SYMBOLS	xiv
1. INTRODUCTION.....	1
1.1 COMPUTATIONAL CHEMISTRY.....	1
1.2 PYRIMIDINE AND ITS DERIVATIVES.....	2
1.3 CANCER, CISPLATIN AND CISPLATIN DERIVATIVES	3
1.4 HOMO-LUMO.....	5
1.5 DIPOLE MOMENT.....	5
1.6 CHEMICAL PROPERTIES	6
1.6.1 Ionization Potential (I).....	6
1.6.2 Electron Affinity (A)	6
1.6.3 Electronegativity (X)	7
1.6.4 Chemical Hardness (H).....	7
1.6.5 Chemical Softness (S).....	7
2. THEORETICAL BACKGROUND	8
2.1 THE SCHRÖDINGER EQUATION	8
2.1.1 Born-Oppenheimer Approximation.....	10
2.2 HARTREE-FOCK THEORY.....	10
2.2.1 Slater Determinant	11
2.2.2 Variational Theorem.....	11
2.2.3 Correlation	12
2.3 DENSITY FUNCTIONAL THEORY	12
2.3.1 Hohenberg-Kohn Theorems	13
2.3.2 The Kohn-Sham Approach.....	13
2.3.3 Exchange-Correlation Functional.....	15
2.3.3.1 Local Density Approximation (LDA).....	15
2.3.3.2 Generalized Gradient Approximation (GGA)	15
2.3.3.2.1 B (BECKE)	15
2.3.3.2.2 Lyp (Lee, Yang And Parr).....	15
2.3.3.3 Hybrid Functionals.....	16
2.3.3.3.1 B3 (3BECKE)	16
2.3.3.3.2 B3LYP.....	16
2.4 BASIS SETS	16
2.4.1 Minimal Basis Sets	17
2.4.2 Split-Valence	17
2.4.3 Diffuse Functions.....	18

2.4.4 Polarization Functions	18
2.4.5 Correlation Consistent Basis Set	19
2.4.5.1 CC-PVDZ	19
2.4.5.2 Aug-CC-PVDZ	19
2.4.6 Effective Core Potentials	19
2.4.6.1 LanL2DZ.....	19
2.4.6.2 SDD.....	19
3. AIM AND SCOPE OF STUDY	20
4. MATERIALS AND METHODS	21
5. RESULT AND DISCUSSION	22
5.1 A COMPUTATIONAL INSIGHT TO THE PYRIMIDINE AND ITS DERIVATIVES IN DNA NUCLEOBASES.....	22
5.1.1 Geometric Properties	22
5.1.1.1 Bond Lengths	22
5.1.1.2 Bond Angles.....	25
5.1.2 Energy Analysis.....	29
5.1.2.1 Total Energy.....	29
5.1.2.2 Dipole Moment	29
5.1.2.3 HOMO-LUMO	31
5.2 NOVEL COMPLEXES OF PLATINUM (II)	34
5.2.1. Geometric Properties	35
5.2.1.1 Bond Lengths	35
5.2.1.1.1 Bond Lengths Of Complexes A And B.....	38
5.2.1.1.2 Bond Lengths Of Complex C.....	39
5.2.1.2 Bond Angles.....	40
5.2.1.2.1 Bond Angles Of Complexes A And B	44
5.2.1.2.2 Bond Angles Of Complex C	45
5.2.1.3 Dihedrals	46
5.2.2 Energy Analysis.....	47
5.2.2.1 Total Energy.....	47
5.2.2.2 Zero Point Energy (ZPE)	48
5.2.3 Dipole Moment.....	49
5.2.4 HOMO-LUMO	49
5.2.5 Chemical Properties.....	53
5.2.5.1 Ionization Potential (I)	53
5.2.5.2 Electron Affinity (A).....	53
5.2.5.3 Electronegativity (X)	54
5.2.5.4 Global Hardness (H) And Global Softness (S)	54
5.3 COMPUTATIONAL INSIGHT TO THE REACTION PATH WAY.....	56
6. CONCLUSION	59
REFERENCES.....	60
7. APPENDICES	66
8. CURRICULUM VITAE.....	82

LIST OF FIGURES

	<u>Page</u>
Figure 1.1. Pyrimidine.	2
Figure 1.2. Adenine.....	2
Figure 1.3. Guanine.....	2
Figure 1.4. Cytosine.	3
Figure 1.5. Thymine.....	3
Figure 1.6. Cisplatin.....	4
Figure 1.7. Carboplatin.	4
Figure 1.8. Oxaliplatin.	4
Figure 1.9. Nedaplatin.....	5
Figure 1.10. Lobaplatin.	5
 Figure 5.1. HOMO-LUMO and Band Gap for Adenine DFT/B3LYP aug-cc-pVDZ Basis set.	 32
Figure 5.2. HOMO-LUMO and Band Gap for Guanine DFT/B3LYP aug-cc-pVDZ Basis set.	 32
Figure 5.3. HOMO-LUMO and Band Gap for Cytosine DFT/B3LYP 6-31G Basis set.	 33
Figure 5.4. HOMO-LUMO and Band Gap for Thymine DFT/B3LYP 6-31G Basis set.	 33
Figure 5.5. Complex A.....	34
Figure 5.6. Complex B.....	34
Figure 5.7. Complex C.....	34
Figure 5.8. Molecular Orbitals Surface for HOMO and LUMO of (A, B and C) Complexes computed at DFT/B3LYP level and 6-311G basis set.....	 52
Figure 5.9. Predicted Reaction pathway of synthesizing complex A.	56
Figure 5.10. Reaction mechanism of synthesizing complex A.....	57
Figure 5.11. Predicted First step of synthesizing complex A.	58
Figure 5. 12. Predicted Second step of synthesizing complex A.	58

LIST OF TABLES

	<u>Page</u>
Table 5.1. Bond Lengths for Pyrimidine Calculated by DFT/B3LYP Level.....	23
Table 5.2. Bond Lengths for Adenine Calculated by DFT/B3LYP Level.	24
Table 5.3. Bond Lengths for Guanine Calculated by DFT/B3LYP Level.	24
Table 5.4. Bond Lengths for Cytosine Calculated by DFT/B3LYP Level.	25
Table 5.5. Bond Lengths for Thymine Calculated by DFT/B3LYP Level.	25
Table 5.6. Pyrimidine Bond Angles ° by DFT/B3LYP.....	26
Table 5.7. Adenine Bond Angles ° by DFT/B3LYP.	27
Table 5.8. Guanine Bond Angles ° by DFT/B3LYP.	27
Table 5.9. Cytosine Bond Angles ° by DFT/B3LYP.	28
Table 5.10. Thymine Bond Angles ° by DFT/B3LYP.	28
Table 5.11. Total Energy E (B3LYP) eV for Pyrimidine and its derivatives in DNA Nucleobases.	29
Table 5.12. Dipole Moment (Debye) of (Pyrimidine, A, G, C and T) calculated using DFT/B3LYP level.....	30
Table 5.13. HOMO-LUMO for Pyrimidine and its derivatives in DNA Nucleobases by DFT/B3LYP Level.....	31
Table 5.14. Bond Lengths for complex A By DFT/B3LYP level.....	36
Table 5.15. Bond Lengths for complex B By DFT/B3LYP level.....	37
Table 5.16. Bond Lengths for complex C by DFT/B3LYP level.	38
Table 5.17. Comparing the calculated bond lengths with cisplatin bond lengths (complex A).	39
Table 5.18. Comparing the calculated bond lengths with cisplatin bond lengths (complex B).	39
Table 5.19. Comparing the calculated bond lengths with cisplatin bond lengths (complex C).	40
Table 5.20. Bond Angles for complex A by DFT/B3LYP level.....	40
Table 5.21. Bond Angles for complex B by DFT/B3LYP level.	41
Table 5.22. Bond Angles for complex C by DFT/B3LYP level.	43
Table 5.23. Comparing the calculated bond Angles with cisplatin bond Angles (complex A).	44

Table 5.24. Comparing the calculated bond Angles with cisplatin bond Angles (complex B).	45
Table 5.25. Comparing the calculated bond Angles with cisplatin bond Angles (complex C).	46
Table 5.26. Dihedrals values of complex A by DFT/B3LYP method.	46
Table 5.27. Dihedrals values of complex B by DFT/B3LYP method.	47
Table 5.28. Dihedrals values of complex C by DFT/B3LYP method.	47
Table 5.29. Total energy (au) of the designed complexes (A, B and C) by DFT/B3LYP level.	48
Table 5.30. Zero-point vibrational energy (Kcal/Mol) of the designed complexes (A, B and C) by DFT/B3LYP level.	48
Table 5.31. Dipole Moment (Debye) of the designed complexes (A, B and C) by DFT/B3LYP level.	49
Table 5.32. HOMO-1, HOMO, LUMO, and LUMO+1 for complexes (A, B and C) by DFT/B3LYP level.	50
Table 5.33. Ionization Potential (I) eV of the Complexes (A, B and C) By DFT/B3LYP level.	53
Table 5.34. Electron Affinity (A) eV of the Complexes (A, B and C) By DFT/B3LYP level.	54
Table 5.35. Electronegativity (A) eV of the Complexes (A, B and C) By DFT/B3LYP level.	54
Table 5.36. Global Hardness (η) and Global softness(S) eV of the Complexes (A, B and C) By DFT/B3LYP level.	55

LIST OF ABBREVIATIONS AND SYMBOLS

ACS	: American Cancer Society
Cisplatin	: Cis-Diamminedichloroplatinum(II)
FDA	: Food And Drug Administration
MOs	: Molecular Orbitals
HOMO	: Highest Occupied Molecular Orbital
LUMO	: Lowest Unoccupied Molecular Orbital
FMOs	: Frontier Molecular Orbitals
HF	: Hartree-Fock Theory
MPn	: Müller-Plesset Perturbation Theory
GVB	: The Generalized Valence Bond Method
MCSCF	: Multi-Configurational Self-Consistent Field
CI	: Configuration Interaction
CC	: Coupled Cluster Theory
DFT	: Density Functional Theory
LDA	: Local Density Approximation
GGA	: Generalized Gradient Approximation
B	: Becke's Exchange Functional
LYP	: Lee, Yang And Parr Correlation Functional
B3	: 3 Becke's Exchange Functional
B3LYP	: Becke's Three-Parameter Exchange Functional And The : Lee-Yang-Parr Correlation Functional
AO	: Atomic Orbitals
STOs	: Slater-Type Orbitals
GTOs	: Gaussian-Type Orbitals
STO-nG	: Minimal Basis Sets
DZ	: Double Zeta
TZ	: Triple Zeta

QZ	: Quadruple Zeta
ECP's	: Effective Core Potentials
DNA	: Deoxyribonucleic Acid
MAPE %	: Mean Of Absolute Percentage Error
%error	: Percent Error
SDD	: Stuttgart/Dresden
LANL2	: Los Alamos National Laboratory 2
I	: Ionization Potential
A	: Electron Affinity
χ	: Electronegativity
η	: Global Hardness
S	: Softness
E_{HOMO}	: Energy Of HOMO
E_{LUMO}	: Energy Of LUMO
$\hat{H}$	: The Hamiltonian Operator
Ψ	: The Wave Function
E	: The Energy
$\hat{T}_n$	: Kinetic Energies Of The Nuclei
$\hat{T}_e$	: Kinetic Energies Of The Electrons
$\hat{V}_{en}$	: Interactions Between The Nuclei And The Electrons
$\hat{V}_{ee}$	: The Electron-Electron Coulomb Interaction
$\hat{V}_{nn}$	: The Nucleus-Nucleus Repulsion
Z	: The Nuclear Charge
M_A	: The Ratio Of Mass Of Nucleus A To The Mass Of An Electron
R_{AB}	: The Distance Between Nuclei A And B
r_{ij}	: The Distance Between Electrons I And J
r_{iA}	: The Distance Between Electron I And Nucleus A
$\hat{H}_{el}$	: Electronic Hamiltonian
Φ_{SD}	: The Slater Determinant

$\rho_0(\vec{r})$	: Ground State Density
$\rho_0(\vec{r})\mathbf{V}_{Ne}\mathbf{d}\vec{r}$	: External Potential And It Is A Unique Functional Of $\rho(\vec{r})$ Electron Density
$T[\rho_0]$	: Kinetic Energy
$E_{ee}[\rho_0]$	: Electron-Electron Energy Functional
$\Psi_i^{KS}(\vec{X}_i)$	: Kohn-Sham Orbitals
$\Psi_i^{KS}(\vec{r}, s)$	: Spin Orbital Obtained From Kohn-Sham Orbital
$\rho_s(\vec{r})$	: Electron Density Of The Non-Interacting System
$\rho_0(\vec{r})$	: Ground State Density
$E[\rho(\vec{r})]$	: Ground State Energy
$T_s[\rho(\vec{r})]$	: Kinetic Energy Of Non-Interacting System
$J[\rho(\vec{r})]$	: Electron-Electron Repulsion Energy
$E_{Ne}[\rho]$	: External Potential
$E_{xc}[\rho(\vec{r})]$	: Exchange-Correlation Energy Functional
$E_x[\rho(\vec{r})]$	: Exchange Term
$E_c[\rho(\vec{r})]$	: Correlation Term

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1. INTRODUCTION

1.1 Computational Chemistry

Since the first applying of the quantum methods in 1927 by Heitler and London for calculating the covalent bond of the hydrogen molecule (Heitler & London, 1927), the computational chemistry field pioneered and Day by day calculating became easier and faster especially by appearing of the computers.

The importance of computational chemistry comes from several reasons starting from its safety, since the dangerous reactions can be done without using any material just using computer, to its cheapness. The computational chemistry gives a good insight to the reaction pathway of the reactions that not have done yet so the chemist can predict the possibility of the reaction, properties and stability of the products or even of the reactants.

Unfortunately, computational chemistry is not completely perfect since there is no equation or function can predict exactly where the electron is, where is going to be, or describe perfectly the behavior of the electron and that is the need of developing new methods which can increase the accuracy of calculations.

After publishing the Schrödinger equation in 1926 by Erwin Schrödinger (Schrödinger, 1926) many scientists tried to add approximation to this equation starting from Born-Oppenheimer approximation in which Born and Oppenheimer assumed that the nuclei do not move, to Hartree and Fock and there central field approximation.

In 1964 Hohenberg and Kohn (Hohenberg & Kohn, 1964) demonstrate the theoretical possibility of DFT but they didn't provide the functional that delivers to the ground state energy. One year later in 1965 Kohn and Sham (Kohn & Sham, 1965) constructed an equation similar to Schrödinger equation called Kohn–Sham equation.

Like Schrödinger equation, Kohn–Sham equation has limitation caused by the Exchange-Correlation energy functional since there is no exact form known for it, so a variety of approximate functionals have been developed to solve this problem like Local Density Approximation (LDA) (Jensen, 2007), Generalized Gradient Approximation (GGA) (Jensen, 2007) and other approximations.

1.2 Pyrimidine and Its Derivatives

Pyrimidine (Figure 1.1) is a six membered ring with nitrogen atoms at positions 1 and 3. Also known as 1,3-diazine. It was first prepared by S. Gabriel and James Colman in 1899 (Brown & Mason, 1962).

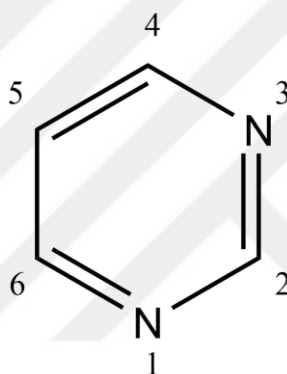


Figure 1.1. Pyrimidine.

The Pyrimidine ring is found in Thiamine (Vitamin B1) (Jain, et al., 2006), Riboflavin (Jain, et al., 2006) and Folic Acid (Jain, et al., 2006). Pyrimidine and fused pyrimidine (Purine) are the most important constituents of Nucleic Acids (Adenine, Guanine, Cytosine and Thymine) as in (Figures 1.2, 1.3, 1.4 and 1.5) respectively.

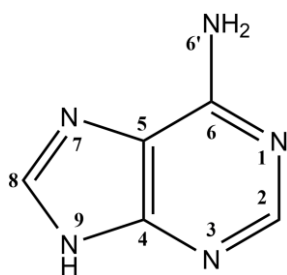


Figure 1.2. Adenine.

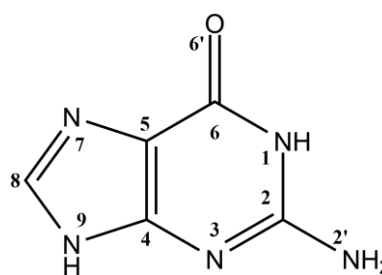


Figure 1.3. Guanine.

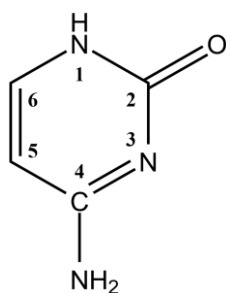


Figure 1.4. Cytosine.

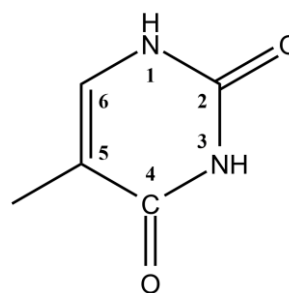


Figure 1.5. Thymine.

Another importance of Pyrimidine is that several Pyrimidine derivatives have been developed as chemotherapeutic agents and have found wide clinical applications (Jain, et al., 2006).

1.3 Cancer, Cisplatin and Cisplatin Derivatives

According to reports from American Cancer Society (ACS), cancer is the third most lethal disease in the world (American Cancer Society., 2007) (Taşkın-Tok & Gowder, 2014). Nearly 13 million people were diagnosed with cancer in 2011. Until now, cancer continues to be a great threat to people (Jemal, et al., 2011) (Taşkın-Tok & Gowder, 2014).

Treatment of cancer involves surgery, radiation and drugs. In drugs treatment the chemotherapy is used, which employs a wide group of drugs with cytotoxic effects. The anticancer drugs stop cell division and proliferation but they don't have perfect selectivity towards cancer cells. Thus, this drugs destroy cancer cells and also destroy normal cells (Taşkın-Tok & Gowder, 2014) and that is the most important reason to develop an anticancer drug with good selectivity and without cytotoxic effects.

Complexes based on Platinum center are important drugs for the treatment of cancer diseases (Foltinová V., 2008). Cisplatin or Cis-diamminedichloroplatinum(II) (Figure 1.6), which is the most important complex of platinum, it is a good anticancer drug that has been in clinical use for almost four decades (Mantri & Baik, 2009).

Cisplatin was discovered by Rosenberg accidentally in 1965 (Rosenberg, Van Camp, & Krigas, 1965) (Mantri & Baik, 2009), cisplatin was approved by Food and

Drug Administration FDA in 1978 (Mantri & Baik, 2009) (Sherman & Lippard, 1987). Since that time, it has become one of the most widely used anticancer drugs, especially in the treatment of ovarian, head-and-neck, testicular and small-cell lung cancers (O'Dwyer, Stevenson, & Johnson, 1999).

Cisplatin is a successful drug, but there are numbers of unsolved problems that limit its value in clinical use, hence, in recent decades a lot of works were devoted to find analogs with improved activity and reduced toxicity (Mantri & Baik, 2009) (Judson & Kelland, 2000) (Wong & Giandomenico, 1999).

Since the discovery of cisplatin hundreds or even thousands of Platinum complexes have been synthesized and evaluated for their anticancer activity (Mantri & Baik, 2009), some of this complexes have entered clinical trials as anticancer agents, unfortunately, few of them have been currently approved, like Carboplatin, worldwide (Figure 1.7), Oxaliplatin in a few countries (Figure 1.8), Nedaplatin in Japan (Figure 1.9), and Lobaplatin in China (Figure 1.10) (Canetta & Lebwohl, 1998) (Mantri & Baik, 2009).

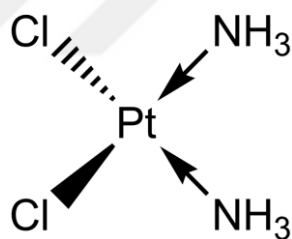


Figure 1.6. Cisplatin.

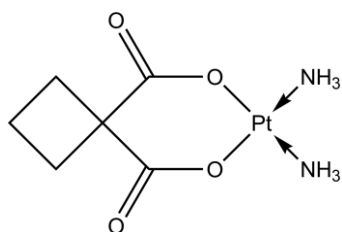


Figure 1.7. Carboplatin.

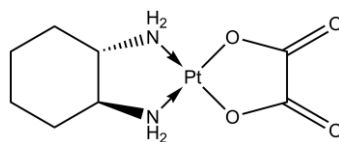


Figure 1.8. Oxaliplatin.

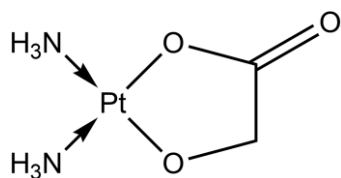


Figure 1.9. Nedaplatin.

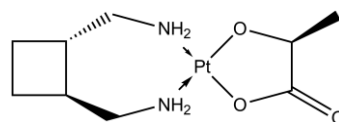


Figure 1.10. Lobaplatin.

A necessary requirement for an active Platinum-based drug seems to be cis coordination of two Amines (Nitrogen) or Bidentate Amine ligands, and two good leaving groups like (SO_4^{2-} , Cl^- , or citrate ... etc.) to Platinum II center (Abu-Surrah & Kettunen, 2006).

Recently, some strategies have arose to synthesize the novel Platinum anticancer drugs. Some of this strategies are based on changing the nitrogen ligand (the Amine group) or changing the leaving groups (the Chlorine group). Other strategies are based on replacing the metal center (e.g. Palladium (II) complexes) (Abu-Surrah & Kettunen, 2006).

1.4 HOMO-LUMO

For the large molecules there is a huge number of molecular orbitals (MOs). But in general the most interesting orbitals are (HOMO and LUMO).

HOMO or the highest occupied molecular orbital witch contain electrons, thus it tends to be an electrons donor, while LUMO or lowest unoccupied molecular orbital is empty and tends to be an electrons acceptor, this orbitals called frontier molecular orbitals (FMOs) developed by Kenichi Fukui in 1952 (Fukui, Yonezawa, & Shingu, 1952). The difference in energy between HOMO and LUMO called HOMO-LUMO band gap energy and it is a very important value for single electron transfer.

1.5 Dipole Moment

Even though the total charge on a molecule is zero, but the positive and negative charges do not completely overlap in most molecules. Such molecule is said

to be polar because it shows a permanent dipole moment. The dipole moment is a property of the molecule that results from charge separation (Smith & March, 2007).

However, it is not possible to measure the dipole moment of an individual bond within a molecule, the total moment of the molecule can be measured only, which is the vectorial sum of the individual bond moments (Smith & March, 2007).

The unit of Dipole moment is Debye in honor of Peter J. W. Debye (1884-1966) who was the first scientist to study the molecular dipoles.

1.6 Chemical Properties

According to Koopman's theorem, Electron Affinity (A), Ionization Potential (I), the Electronegativity (χ), Softness (S) and Global Hardness (η), may be defined in terms of the energy of the HOMO and the LUMO orbitals (Koopmans, 1933).

1.6.1 Ionization Potential (I)

The energy necessary to remove an electron from the neutral atom is called the ionization potential or ionization energy. Ionization potential is related to the energy of the E_{HOMO} (Frisch & Foresman, 1995) (Udhayakala, 2014) through the equation (1.1):

$$I = -E_{\text{HOMO}} \quad (1.1)$$

1.6.2 Electron Affinity (A)

The energy released from neutral atom when an electron added to form a negative ion is called the Electron Affinity. Electron Affinity is related to the energy of E_{LUMO} (Frisch & Foresman, 1995) (Udhayakala, 2014) through the equation (1.2):

$$A = -E_{\text{LUMO}} \quad (1.2)$$

1.6.3 Electronegativity (χ)

The tendency of an atom, molecule or a functional group to withdrawing electrons towards itself is called Electronegativity (χ). It is related to the Ionization potential (I) and Electron affinity (A) (Pauling, 1960) through the equation (1.3)

$$\chi = \frac{I+A}{2} \quad (1.3)$$

1.6.4 Chemical Hardness (η)

The resistance of an atom to charge transfer is called Chemical Hardness (η) (Senet, 1997). It is related to the Ionization potential (I) and Electron affinity (A) (Udhayakala, 2014) through the equation (1.4):

$$\eta = \frac{I-A}{2} \quad (1.4)$$

1.6.5 Chemical Softness (S)

Chemical softness (S), is reverse of the hardness (Senet, 1997), and it is related to Chemical Hardness (η) (Udhayakala, 2014) through the equation (1.5):

$$S = \frac{1}{\eta} \quad (1.5)$$

2. THEORETICAL BACKGROUND

Classical mechanic was quite powerful in helping scientists to understand everyday phenomena, but unfortunately it has been found to be unhelpful in the limit of light-like speeds, the vicinity of ultra-heavy objects and on atomic length scales. So it had to be replaced by the theories of quantum mechanics which were promising theories to solve these problems.

By using Quantum Mechanics, it is possible to predict, correlate and describe the behavior of a great range of physical systems, starting from particles through nuclei and atoms to molecules (Merzbacher, 1998). Quantum Mechanics describe the behavior of the electrons mathematically (i.e. by equations).

Until now the equations of quantum mechanical methods have never been solved exactly or completely for any system other than the hydrogen atom. So, the field of quantum mechanics is mainly built around approximate solutions. Some of these approximate solutions are expected to be more accurate than any experiment and others are very crude (Young, 2001).

2.1 The Schrödinger Equation

The fundamental equation of theoretical chemistry is The Schrödinger Equation. It was formulated in late 1925 and published in 1926 by the Austrian physicist Erwin Schrödinger (Schrödinger, 1926) describing the electron as a wave. It is also often called the Schrödinger wave equation (Jensen, 2007) (Koch & Holthausen, 2001). Time-independent Schrödinger equation (2.1):

$$\hat{H}\Psi(r) = E\Psi(r) \quad (2.1)$$

Where:

- $\hat{H}$: The Hamiltonian operator.
- Ψ : The wave function.

- E : The energy, eigenvalue of the Hamiltonian operator.

The Hamiltonian operator can be described as a sum of kinetic and potential energies of the nuclei and electrons by equation (2.2):

$$\hat{H} = \hat{T}_n + \hat{T}_e + \hat{V}_{en} + \hat{V}_{ee} + \hat{V}_{nn} \quad (2.2)$$

Where:

- $\hat{T}_n$, $\hat{T}_e$: operators represent the kinetic energies of the nuclei ($\hat{T}_n$) and electrons ($\hat{T}_e$).
- $\hat{V}_{en} + \hat{V}_{ee} + \hat{V}_{nn}$: represent the interactions between the nuclei and the electrons ($\hat{V}_{en}$), the electron-electron Coulomb interaction ($\hat{V}_{ee}$) and the nucleus-nucleus repulsion term ($\hat{V}_{nn}$).

The mathematical representation of the Hamiltonian operator $\hat{H}$ can be written as equation (2.3):

$$\hat{H} = -\frac{1}{2} \sum_i^{electrons} \nabla_i^2 - \frac{1}{2} \sum_A^{nuclei} \frac{1}{M_A} \nabla_A^2 - \sum_i^{electrons} \sum_A^{nuclei} \frac{Z_A}{r_{iA}} + \sum_{i < j}^{electrons} \sum_j \frac{1}{r_{ij}} + \sum_{A < B}^{nuclei} \sum_B \frac{Z_A Z_B}{R_{AB}} \quad (2.3)$$

Where:

- Z: The nuclear charge.
- M_A : The ratio of mass of nucleus A to the mass of an electron.
- R_{AB} : The distance between nuclei A and B.
- r_{ij} : The distance between electrons i and j.
- r_{iA} : The distance between electron i and nucleus A.

Schrödinger equation cannot be solved exactly for the many-electron systems (or at least has not been solved) even for the simplest two-electron systems such as helium atom or hydrogen molecule. Approximations need to be introduced to provide practical methods (Hegre W. , 2003).

2.1.1 Born-Oppenheimer Approximation

Schrödinger Equation for molecular systems can be simplified by assuming that the nuclei do not move, Of course they do, but the motion of nuclei is “very slow” compared to the speed of electrons. This is called the Born-Oppenheimer approximation (Born & Oppenheimer, 1926) and leads to an Electronic Schrödinger Equation (Koch & Holthausen, 2001) as equation (2.4):

$$\hat{H}_{el}\Psi_{el} = E_{el}\Psi_{el} \quad (2.4)$$

The electronic Hamiltonian can be written as equation (2.5):

$$\hat{H}_{el} = -\frac{1}{2} \sum_i^{electrons} \nabla_i^2 - \sum_i^{electrons} \sum_A^{nuclei} \frac{Z_A}{r_{iA}} + \sum_{i<j}^{electrons} \sum_j \frac{1}{r_{ij}} \quad (2.5)$$

2.2 Hartree-Fock Theory

Hartree-Fock (HF) theory (Hartree, 1928) (Fock, 1930) is the simplest wavefunction-based method in which the central field approximation is the primary approximation, and that means the coulombic electron-electron repulsion is taken into account by integrating the repulsion term. This gives the average effect of the repulsion, but not the explicit repulsion interaction. The approximate energies calculated are equal to or greater than the exact energy and that is called a variational calculation. Thus, the energies from HF calculations are always greater than the exact energy and tend to a limiting value called the Hartree-Fock limit as the basis set is improved (Young, 2001).

HF method breaks the many-electron Schrödinger equation into many simpler one-electron equations and that is one of its advantages. So, solving one electron equation yields a single-electron wave function called an orbital, and an energy called an orbital energy. The orbital describes the behavior of an electron in the net field of all the other electrons. The energies are calculated in units called Hartrees (1 Hartree = 27.2116 eV).

2.2.1 Slater Determinant

Two electrons cannot have the same set of quantum numbers (Pauli Exclusion Principle) (Pauli, 1925).

The electrons are fermions and the interchange of any two electrons brings about a change in the sign of the wave function Ψ , i.e. the function is Antisymmetric (Koch & Holthausen, 2001) as equation (2.6):

$$\Psi(\vec{x}_1, \vec{x}_2) = -\Psi(\vec{x}_2, \vec{x}_1) \quad (2.6)$$

Both the spatial and the spin coordinates are encountered as equation (2.7):

$$\vec{x}_i = (\vec{r}_i, r_i) \quad (2.7)$$

The Slater Determinant ϕ_{SD} can be used to express the appropriate functional form of the ground state (Ψ_0) of a polyelectronic system with N number of electrons and $\chi_1, \chi_2, \dots, \chi_N$ spin orbitals, satisfying the antisymmetry principle as equation (2.8):

$$\Psi_0 \approx \phi_{SD} = \frac{1}{N!} \begin{vmatrix} \chi_1(\vec{x}_1) & \chi_2(\vec{x}_1) & \dots & \chi_N(\vec{x}_1) \\ \chi_1(\vec{x}_2) & \chi_2(\vec{x}_2) & \dots & \chi_N(\vec{x}_2) \\ \vdots & \vdots & & \vdots \\ \chi_1(\vec{x}_N) & \chi_2(\vec{x}_N) & & \chi_N(\vec{x}_N) \end{vmatrix} \quad (2.8)$$

The one-electron functions $\chi_i(\vec{x}_i)$ are called spin orbitals, and are composed of a spatial orbital $\phi_i(\vec{r})$ and one of the two spin functions, $\alpha(s)$ or $\beta(s)$ as equation (2.9):

$$\chi(\vec{x}) = \phi(\vec{r})\sigma(s) \quad \sigma = \alpha, \beta \quad (2.9)$$

2.2.2 Variational Theorem

The exact wave function is not known, so, an approximate wave function (Ψ_{approx}) has to be used. Consequently, an approximate energy E_{approx} will be obtained instead of calculating exact energy E_{exact} . Hence, the Variational Theorem state that approximate energy will be equal or greater than exact energy (Koch & Holthausen, 2001).

2.2.3 Correlation

In HF theory, only the distance of an electron from the nucleus is determining the probability of finding this electron around the atom, that mean the distance to the other electrons is not considered. This is not physically true, but that is the result of the central field approximation, which defines the HF method.

One of the limitations of HF is taking into account the average effect of electron repulsion, instead of the explicit electron-electron interaction, and as a consequence the calculations do not include electron correlation (Young, 2001). The next calculations (methods) are calculations begin with a HF calculation and then correct for correlation and called (correlated calculations):

- Coupled Cluster Theory (CC).
- The Generalized Valence Bond (GVB) method.
- Configuration Interaction (CI).
- Multi-Configurational Self-Consistent Field (MCSCF).
- Müller-Plesset Perturbation Theory (MPn, n is the order of correction).

Correlation generally increases the accuracy of the computed molecular geometries and the computed energies.

2.3 Density Functional Theory

The energy of a molecule can be determined by using the electron density instead of a wave function and that is the core of Density Functional Theory (DFT).

The main two fundamental mathematical theorems of Density Functional Theory are provided by Kohn and Hohenberg (applied only to finding the ground-state electronic energy of a molecule) and Kohn and Sham with their derivation of a set of equations (they formulated a method similar in structure to the Hartree-Fock method) (Young, 2001).

2.3.1 Hohenberg-Kohn Theorems

Hohenberg and Kohn derived two theorems, which laid to the foundations of the Density Functional Theory.

The first theorem, called the “Existence” theorem, states that “the ground-state energy from Schrodinger’s equation is a unique functional of the electron density” (Hohenberg & Kohn, 1964) (Sholl & Steckel, 2009). The energy of a system E_0 is a functional (a function of function) of its density so it can be expressed as equation (2.10) (Hohenberg & Kohn, 1964):

$$E_0 = E_0[\rho_0] = \int \rho_0(\vec{r}) V_{Ne} d\vec{r} + T[\rho_0] + E_{ee}[\rho_0] \quad (2.10)$$

Where:

- $\rho_0(\vec{r})$: Ground state density.
- $\rho_0(\vec{r}) V_{Ne} d\vec{r}$: External Potential and it is a unique functional of $\rho(\vec{r})$ Electron Density.
- $T[\rho_0]$: Kinetic energy.
- $E_{ee}[\rho_0]$: Electron-electron energy functional.

The second theorem of Hohenberg–Kohn defines an important property of the functional: “the electron density that minimizes the energy of the overall functional is the true electron density corresponding to the full solution of the Schrödinger equation” (Hohenberg & Kohn, 1964) (Sholl & Steckel, 2009).

2.3.2 The Kohn-Sham Approach

Even though the Hohenberg–Kohn theorem confirmed the theoretical possibility of the DFT and proof that the mapping between the ground state density $\rho_0(\vec{r})$ and the ground state energy E_0 exists in principle, but they did not provide any guidance at how the functional that delivers to the ground state energy should be constructed, and that what Kohn and Sham did (Kohn & Sham, 1965).

The Kohn and Sham idea was realizing that if it is not able to accurately determine the kinetic energy through an explicit functional, so computing as much as

possible of the true kinetic energy should be concentrated. So the remainder in an approximate manner have to be dealt with (Koch & Holthausen, 2001).

A molecule with N-electron density can be separated into N one-electron density packets or orbitals known as Kohn-Sham Orbitals $\Psi_i^{KS}(\vec{X}_i)$ as equation (2.11):

$$\rho_s(\vec{r}) = \sum_i^N \sum_s |\Psi_i^{KS}(\vec{r}, s)|^2 = \rho_0(\vec{r}) \quad (2.11)$$

Where:

- $\Psi_i^{KS}(\vec{r}, s)$: Spin orbital obtained from Kohn-Sham orbital.
- $\rho_s(\vec{r})$: Electron density of the non-interacting system.
- $\rho_0(\vec{r})$: Ground state density.

Ground state energy $E[\rho(\vec{r})]$ of molecular system can be represented as equation (2.12):

$$E[\rho(\vec{r})] = T_s[\rho(\vec{r})] + J[\rho(\vec{r})] + E_{XC}[\rho(\vec{r})] + E_{Ne}[\rho] \quad (2.12)$$

Where:

- $T_s[\rho(\vec{r})]$: Kinetic energy of non-interacting system.
- $J[\rho(\vec{r})]$: Electron-Electron repulsion energy.
- $E_{Ne}[\rho]$: External potential.
- $E_{XC}[\rho(\vec{r})]$: Exchange-Correlation energy functional.

Exchange-Correlation energy functional $E_{XC}[\rho(\vec{r})]$ include all terms that cannot be accurately obtained and it is usually calculated as sum of exchange term $E_X[\rho(\vec{r})]$ and correlation term $E_C[\rho(\vec{r})]$ as equation (2.13):

$$E_{XC}[\rho(\vec{r})] = E_X[\rho(\vec{r})] + E_C[\rho(\vec{r})] \quad (2.13)$$

The exact form of $E_{XC}[\rho(\vec{r})]$ term is not known. So a variety of approximate functionals have been developed.

2.3.3 Exchange-Correlation Functional

The difference between various DFT methods is the functional form of the exchange–correlation energy. $E_{xc}[\rho(\vec{r})]$ is valid for all systems and it is a unique functional, but a clear and ideal functional form of this potential has not been constructed. And the next functionals represent different approximations to the exchange-correlation functional.

2.3.3.1 Local Density Approximation (LDA)

In the Local Density Approximation (LDA), it is assumed that the local density can be treated as a uniform electron gas, or equivalently that the density is a slowly varying function (Jensen, 2007).

2.3.3.2 Generalized Gradient Approximation (GGA)

The LDA can be considered as a zeroth order approximation, but it is not good enough so a new type of functional was introduced called the generalized gradient approximation. These functionals include the gradient of the electron density.

Here some of the most efficient GGA functionals commonly used in computational chemistry (Jensen, 2007).

2.3.3.2.1 B (Becke)

It is an exchange functional developed by Becke (Becke, 1988), it is a gradient correction to the LDA exchange energy. Becke's Exchange Functional includes a single parameter fitted on known atomic data from the rare gas atoms (Jensen, 2007).

2.3.3.2.2 LYP (Lee, Yang and Parr)

It is a correlation functional developed by Lee, Yang and Parr (Lee, Yang, & Parr, 1988). It is the most extensively used GGA correlation functional. It contains four empirical parameters fitted to the helium atom (Jensen, 2007).

2.3.3.3 Hybrid functionals

An alternative approach would be to use a mix of DFT and HF to describe the exchange energy. Usually hybrid functionals are composed of a mixture of exact and DFT exchange. The main element of these functionals comes from GGA functionals, so they are often called GGA hybrid functionals (Jensen, 2007) (Perdew, Ernzerhof, & Burke, 1996), like:

2.3.3.3.1 B3 (3Becke)

Contains exact exchange, and is an exchange functional developed by Becke. It is a combination of LDA and GGA functionals (Becke, Density functional thermochemistry. III. The role of exact exchange, 1993).

2.3.3.3.2 B3LYP

A famous example of exchange and correlation combination is The B3LYP functional, it is a mix between Becke's three-parameter exchange functional (Becke, 1993) and the Lee-Yang-Parr correlation functional (Lee, Yang, & Parr, 1988), first suggested by Becke (Becke, 1993)

2.4 Basis Sets

The set of functions that used to describe the shape of molecular orbitals (MOs) or atomic orbitals (AOs) are called basis sets. The linear combinations of the basic functions and angular functions are the main process to create the molecular orbitals. This basis functions can be classified into two main types:

- Gaussian-type orbitals, also known as GTOs.
- Slater-type orbitals, also called STOs.

2.4.1 Minimal Basis Sets

The Minimal Basis Sets are primarily used to take a “first look” at one or more molecular properties, but they consider all electrons as being of equal importance. The most common one is STO-nG (Hehre, Stewart, & Pople, 1969).

For an example the smallest minimal basis set is STO-3G (Collins, Schleyer, Binkley, & Pople, 1976) which described by a single STO-type which itself approximated by 3 GTO-type.

2.4.2 Split-Valence

The minimal basis sets (STO-nG) consider all electrons to be equal and that is one of the major problems with this family of basis sets. In fact, the outer shell electrons (“valence electrons”) and the inner shell electrons (“core electrons”) are not equivalent, a method to differentiate between electrons in the 1s, 2s, 2p, and other orbitals is required. A solution to this problem is to perform a very rough calculation of the contribution of the core electrons, and a more rigorous calculation of the valence electrons. This type of basis set is known as a “split-valence” basis set. Doubling the number of STOs can improve the accuracy of the STO calculations. These kinds of basis sets are known as “double zeta (DZ)” basis sets. There are also triple and quadruple zeta (TZ, QZ) basis sets.

The 3-21G basis set is an example of split-valence basis set (Herre, Ditchfield, & Pople, 1972), in this basis set the GTO will be used to approximate the STO, there are two parts in this notation “firstnumber-secondnumberG”:

- The first number is “3” and it means a Slater equation will be used to approximate the core electrons using STO-3G basis set.
- The second number “21” it means a double zeta approximation will be used for the valence electrons. So, each of the electrons in the valence orbital will be calculated twice. In the first time, the valence electron(s) calculations will be done using a STO-2G basis set, then re-calculation will be done to the valence electrons with a single STO-1G basis set.

The 6-311G basis set is an example of triple zeta (Krishnan, Binkley, Seeger, & Pople, 1980) (McLean & Chandler, 1980).

2.4.3 Diffuse Functions

The highest probability of finding the electrons is the near of the nucleus, and this probability will be decreasing by increasing the distance from the nucleus, as a result, calculations may stop at larger distances from the nucleus, because typically the electrons won't be found there. In some systems like atoms in the excited states and anions, diffuse function may be used (Clark, Chandrasekhar, Spitznagel, & Schleyer, 1983) to stretch the distance of finding electrons away from the nucleus. "+" symbol or "++" symbol added to the basis set to indicate the diffuse function.

2.4.4 Polarization Functions

Polarization takes into account sometimes when some electrons might occasionally "stray" from its orbital into another orbital (Frisch, Pople, & Binkley, 1984). Polarization gives more accurate description of where the electron is and where the electron can go. A polarized basis set is indicated by "*" in some places, or by the orbital name in others, like 3-21G* basis set or a 3-21G(d) basis set. Where:

"*" or "d" on only heavy atoms (i.e. non-hydrogen atoms).

"" or "dp" includes diffuse functions for all atoms (i.e. all atoms and hydrogen atom).

Examples

A basis set like 3-21+G(d) would be a polarized diffuse split-valence basis set which includes diffuse functions.

A basis set like 6-31G (Herre, Ditchfield, & Pople, 1972) would be a split-valence basis set with no polarization nor diffusion.

2.4.5 Correlation Consistent Basis Set

2.4.5.1 cc-pVDZ

Correlation consistent polarized valence double-zeta basis set (Dunning, 1989) is proposed for all of the first row atoms from boron through neon.

2.4.5.2 Aug-cc-pVDZ

The augmented correlation-consistent polarized valence double-zeta basis set (Kendall, Dunning, & Harrison, 1992).

2.4.6 Effective Core Potentials

Effective core potentials (ECP's) have been generated to replace the innermost core electron for the large atoms with approximate pseudo potential (the core electrons are almost ignored) (Kahn & Goddard, 1972). The electrons in the outermost occupied shell are determine many chemical properties like bond strengths, electron affinities, and ionization potentials.

2.4.6.1 LANL2DZ

The Los Alamos National Laboratory basis sets developed by Hay and Wadt (Hay & Wadt, 1985) (Wadt & Hay, 1985) (Hay & Wadt, 1985).

2.4.6.2 SDD

Stuttgart/Dresden ECPs Effective core potentials basis set.

3. AIM AND SCOPE OF STUDY

The aim of this work is to investigate the derivatives of pyrimidine with DNA nucleobases (Adenine, guanine, Cytosine, Thymine) computationally using Quantum Mechanical Methods and compare the obtained results with the experimental data. Moreover, designed and optimized novel complexes of Platinum (II) (based on cisplatin anticancer drug) will be investigated computationally using Quantum Mechanical Methods too and the quantum chemical properties of these complexes will be studied and discussed. Finally, the theoretical prediction of reaction pathway of one of the complexes will be studied too.

4. MATERIALS AND METHODS

All Computational calculations in this work were performed by Gauss-View 5.0.9 molecular visualization program, and Gaussian 09W v8.0 Rev B.01 SMP program package, and using HP (Hewlett-Packard) Notebook - 15-g210nt (AMD Quad-Core A4-6210 APU with Radeon R3 Graphics (1.8 GHz, 2 MB cache) of microprocessor) and (4 GB 1333 MHz DDR3L SDRAM (1 x 4 GB) of memory).

The methods used for calculation in this work is DFT/B3LYP and several basis sets as explained above (2.3 and 2.4).

5. RESULT AND DISCUSSION

5.1 A Computational Insight to the Pyrimidine and Its Derivatives in DNA Nucleobases

The calculations of Pyrimidine and its derivatives in DNA nucleobases (Adenine, Guanine, Cytosine, and Thymine) were conducted by Density Functional Theory and several basis sets. The bond lengths, bond angles, dipole moment, total energy, HOMO and LUMO will be discussed, the HOMO-LUMO band gap of the nucleobases will be discussed too.

For more calculation results for bond angles and bond lengths using HF method see Appendices (A and B).

5.1.1 Geometric Properties

In theoretical calculations difference basis sets give difference results thus difference accuracy.

The structures of Pyrimidine and its derivatives in DNA nucleobases have been optimized by Density Functional Theory using B3LYP (Becke's three-parameter exchange functional and the Lee-Yang-Parr correlation functional) level and (3-21G, 6-31G, 6-31G++dp, and aug-cc-pVDZ) basis sets.

5.1.1.1 Bond Lengths

All bond lengths of the Pyrimidine and its derivatives in DNA compared with the experimental bond lengths taken from ref (L. Fernhold, 1978) and (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004).

By comparing the calculated bond lengths of Pyrimidine (Table 5.1) with the experimental data the aug-cc-pVDZ basis set showed a good accuracy with 0.32% of (MAPE %) (Mean of Absolute Percentage Error, Appendix F) and for (3-21G, 6-31G

and 6-31G++dp) basis sets the results were 0.93%, 0.99% and 0.47% of (MAPE %) respectively.

For Adenine (Table 5.2) 6-31G++dp basis set showed the best accuracy with 0.52% of (MAPE %) and for (3-21G, 6-31G and aug-cc-pVDZ) basis sets the results were 0.89%, 0.98% and 0.54% of (MAPE %) respectively.

For Guanine (Table 5.3) 6-31G++dp basis set showed the best accuracy too with 1.14% of (MAPE %) and for (3-21G, 6-31G and aug-cc-pVDZ) basis sets the results were 1.21%, 1.23% and 1.17% of (MAPE %) respectively.

Moreover for Cytosine (Table 5.4) 6-31G and 6-31G++dp basis sets showed the best accuracy with 1.27% of (MAPE %) and for (3-21G and aug-cc-pVDZ) basis sets the results were 1.39% and 1.28% of (MAPE %) respectively.

Finally, for Thymine (Table 5.5) 6-31G++dp and aug-cc-pVDZ basis sets showed the best accuracy with almost 0.8% of (MAPE %) and for (3-21G and 6-31G) basis sets the results were 1.2% and 1.36% of (MAPE %) respectively.

Table 5.1. Bond Lengths for Pyrimidine Calculated by DFT/B3LYP Level.

Bond Lengths for Pyrimidine Calculated by DFT/B3LYP Level					
Bond	Exp ^a	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.34	1.3498	1.3509	1.3386	1.3388
C2-N3	1.34	1.3498	1.3509	1.3386	1.3388
N3-C4	1.34	1.3524	1.3538	1.3399	1.3396
C4-C5	1.393	1.3947	1.3981	1.3945	1.3954
C5-C6	1.393	1.3947	1.3981	1.3945	1.3954
C6-N1	1.34	1.3524	1.3538	1.3399	1.3396
C2-H	1.099	1.0824	1.0823	1.0873	1.0916
C4-H	1.099	1.0842	1.0846	1.0881	1.0929
C5-H	1.099	1.0819	1.0836	1.0849	1.0897
C6-H	1.099	1.0842	1.0846	1.0881	1.0929
MAEP%		0.93	0.99	0.47	0.32

Exp^a: (L. Fernhold, 1978).

Table 5.2. Bond Lengths for Adenine Calculated by DFT/B3LYP Level.

Bond Lengths for Adenine Calculated by DFT/B3LYP Level.					
Bond	Exp^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.339	1.352	1.355	1.3445	1.3449
C2-N3	1.331	1.35	1.35	1.3373	1.3372
N3-C4	1.344	1.345	1.35	1.3395	1.3401
C4-C5	1.383	1.403	1.404	1.3993	1.4004
C5-C6	1.406	1.407	1.41	1.4117	1.4123
C6-N1	1.351	1.355	1.359	1.3457	1.3457
C5-N7	1.388	1.4	1.399	1.3856	1.3869
N7-C8	1.311	1.325	1.325	1.3121	1.3128
C8-N9	1.373	1.397	1.393	1.3811	1.3816
N9-C6	1.374	1.385	1.383	1.3782	1.3789
C6-N6	1.335	1.349	1.354	1.3542	1.3556
MAPE%		0.89	0.98	0.52	0.54

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004).

Table 5.3. Bond Lengths for Guanine Calculated by DFT/B3LYP Level.

Bond Lengths for Guanine Calculated by DFT/B3LYP Level.					
Bond	Exp^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.373	1.3773	1.3818	1.372	1.3715
C2-N3	1.323	1.3243	1.3271	1.3126	1.3129
N3-C4	1.35	1.3585	1.3648	1.3585	1.3594
C4-C5	1.379	1.3979	1.4005	1.3962	1.3974
C5-C6	1.419	1.4316	1.4327	1.4398	1.441
C6-N1	1.391	1.4563	1.444	1.4377	1.4368
C5-N7	1.388	1.3988	1.3967	1.3818	1.3834
N7-C8	1.305	1.3208	1.3223	1.3087	1.3094
C8-N9	1.374	1.4037	1.3981	1.3857	1.3862
N9-C4	1.375	1.3766	1.376	1.3701	1.3709
C2-N2	1.341	1.3609	1.3646	1.3762	1.3778
C6-O6	1.237	1.2329	1.2435	1.2212	1.2198
MAPE%		1.21	1.23	1.14	1.17

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004)

Table 5.4. Bond Lengths for Cytosine Calculated by DFT/B3LYP Level.

Bond Lengths for Cytosine Calculated by DFT/B3LYP Level.					
Bond	Exp ^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.399	1.4492	1.4355	1.4272	1.4257
C2-N3	1.356	1.3796	1.3803	1.3705	1.3707
N3-C4	1.334	1.3232	1.3327	1.3217	1.3227
C4-C5	1.426	1.4429	1.4432	1.442	1.4415
C5-C6	1.337	1.3584	1.3632	1.3605	1.3619
C6-N1	1.364	1.361	1.3654	1.3562	1.3554
C2-O2	1.237	1.2326	1.2441	1.2241	1.2235
C4-N4	1.337	1.3588	1.3614	1.3594	1.3604
MAPE%		1.39	1.27	1.27	1.28

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004)

Table 5.5. Bond Lengths for Thymine Calculated by DFT/B3LYP Level.

Bond Lengths for Thymine Calculated by DFT/B3LYP Level.					
Bond	Exp ^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.376	1.399	1.3931	1.3879	1.3875
C2-N3	1.373	1.393	1.389	1.3847	1.3846
N3-C4	1.382	1.413	1.4104	1.4071	1.4069
C4-C5	1.445	1.467	1.4666	1.4685	1.4684
C5-C6	1.339	1.349	1.3574	1.3539	1.3547
C6-N1	1.378	1.384	1.3868	1.3813	1.3812
C2-O2	1.22	1.232	1.2432	1.2214	1.2204
C4-O4	1.228	1.239	1.2479	1.2246	1.2232
C5-Me5	1.496	1.51	1.5076	1.5015	1.5012
MAPE%		1.2	1.36	0.807	0.808

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004).

5.1.1.2 Bond Angles

All bond angles of the Pyrimidine and its derivatives in DNA compared with the experimental bond angles taken from ref (L. Fernhold, 1978) and (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004) too.

By comparing Pyrimidine bond angles with experimental data (Table 5.6) the basis sets 6-31G++dp and aug-cc-pVDZ showed the best accuracy with almost 0.3%

of (MAPE %) and for 3-21G and 6-31G basis sets the results were less accurate with almost 0.6% (MAPE %).

In the case of Adenine (Table 5.7) 6-31G++dp and aug-cc-pVDZ basis sets showed the best accuracy with (MAPE %) near to 0.6%, while the (MAPE %) was 0.78% and 0.67% for 3-21G and 6-31G basis sets respectively.

For Guanine (Table 5.8) 6-31G++dp and aug-cc-pVDZ basis sets were the highest in accuracy with 0.57% and 0.58 of (MAPE %) respectively, while it was 0.91% and 0.75% for 3-21G and 6-31G basis sets respectively.

Also, in Cytosine (Table 5.9) 6-31G basis set gave the best accuracy with 1.3% of (MAPE %) and it was 1.42% with 6-31G++dp and aug-cc-Pvdz basis sets, while it was 1.49% with 3-21G basis set.

Finally, for Thymine (Table 5.10) 6-31G basis set showed best accuracy with 0.66% of (MAPE %), while it was 1.08%, 0.71% and 0.7% with 3-21G, 6-31G++dp and aug-cc-pVDZ basis sets respectively.

Table 5.6. Pyrimidine Bond Angles ° by DFT/B3LYP.

Pyrimidine Bond Angles ° by DFT/B3LYP					
Angle	Exp ^a	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2-N3	127.6	126.0525	126.0107	127.0438	127.1175
C2-N3-C4	115.5	116.4093	116.5366	115.9533	115.9475
N3-C4-C5	122.3	122.0272	121.8906	122.2660	122.1984
C4-C5-C6	116.8	117.0745	117.1349	116.5176	116.5906
C5-C6-N1	122.3	122.0273	121.8906	122.2660	122.1984
C6-N1-C2	115.5	116.4092	116.5366	115.9533	115.9475
N1-C2-H	116.2	116.9736	116.9947	116.4781	116.4413
C5-C4-H	122.4	121.1553	121.7215	121.2834	121.1934
C6-C5-H	121.6	121.4627	121.4326	121.7412	121.7047
MAEP%		0.58	0.59	0.309	0.308

Exp^a: (L. Fernhold, 1978).

Table 5.7. Adenine Bond Angles ° by DFT/B3LYP.

Adenine Bond Angles ° by DFT/B3LYP.					
Angle	Exp^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N7-C8-N9	113.8	112.4349	112.572	113.2757	113.2289
C8-N7-C5	103.9	104.5678	104.5244	104.1013	104.1659
N7-C5-C6	132.3	132.2	132.3504	132.7187	132.7779
N7-C5-C4	110.7	111.0235	110.8559	111.3329	111.2581
C6-C5-C4	117	116.7765	116.7937	115.9483	115.964
C5-C6-N6	123.7	122.2142	122.7736	122.4099	122.3929
C5-C6-N1	117.7	118.6677	118.4978	118.6925	118.7007
N6-C6-N1	118.6	119.1181	118.7287	118.8977	118.9064
C6-N1-C2	118.6	118.7799	118.8837	118.6222	118.5843
N1-C2-N3	129.3	127.6023	127.6547	128.5601	128.6375
C2-N3-C4	110.6	112.2482	112.1098	111.3928	111.3802
C5-C4-N3	126.8	125.9254	126.0603	126.784	126.7332
C5-C4-N9	105.8	104.9761	105.0365	104.5364	104.5507
N3-C4-N9	127.4	129.0986	128.9031	128.6796	128.7161
C8-N9-C4	105.8	106.9978	107.0112	106.7537	106.7964
MAEP%		0.78	0.67	0.59	0.6

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004).**Table 5.8.** Guanine Bond Angles ° by DFT/B3LYP.

Guanine Bond Angles ° by DFT/B3LYP					
Angle	Exp^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N7-C8-N9	113.1	111.7734	112.0451	112.721	112.6426
C8-N7-C5	104.3	105.2192	105.0618	104.6659	104.7541
N7-C5-C6	130.4	129.7604	130.2073	130.4984	130.593
N7-C5-C4	110.8	110.4764	110.4189	110.8917	110.8043
C6-C5-C4	118.8	119.7631	119.3738	118.6078	118.6013
C5-C6-O	128.6	131.8166	130.9266	131.2404	131.2865
C5-C6-N1	111.5	109.4307	110.2452	109.6786	109.6013
O-C6-N1	119.9	118.7527	118.8282	119.0798	119.1116
N1-C2-N3	123.9	122.8885	122.9097	123.4123	123.4957
N3-C2-N2	119.9	118.9348	119.0722	119.5378	119.5049
N1-C2-N2	116.2	118.1767	118.0181	117.0024	116.9515
C2-N3-C4	111.9	113.4747	113.4557	112.7448	112.6176
N3-C4-C5	128.6	128.3058	128.0973	129.0895	129.1165
C5-C4-N9	105.4	105.5447	105.5321	104.9926	104.9927
N3-C4-N9	126	126.1495	126.3706	125.9138	125.8876
C8-N9-C4	106.4	106.9862	106.9421	106.7287	106.8063
C6-N1-C2	125.1	126.1373	125.9184	126.4564	126.5583
MAEP%		0.91	0.75	0.57	0.58

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004).

Table 5.9. Cytosine Bond Angles ° by DFT/B3LYP.

Cytosine Bond Angles ° by DFT/B3LYP					
Angle	Exp ^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
C6-N1-C2	120.3	123.0157	123.1371	123.2704	123.3625
N1-C6-C5	121	120.4583	120.0608	119.9773	119.9409
C6-C5-C4	117.4	116.4074	116.6508	116.1205	116.0693
C5-C4-N4	120.2	119.3951	119.839	119.1517	119.1425
C5-C4-N3	121.9	123.4935	123.3163	123.9145	123.9664
N4-C4-N3	118	117.1114	116.8446	116.9338	116.891
C4-N3-C2	119.9	121.4549	120.8383	120.3583	120.2756
N1-C2-N3	119.2	115.1702	115.9967	116.359	116.3853
N1-C2-O	118.9	118.5016	118.4822	118.1222	118.1524
N3-C2-O	121.9	126.3282	125.5212	125.5188	125.4623
MAEP%		1.49	1.3	1.42	1.42

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004)

Table 5.10. Thymine Bond Angles ° by DFT/B3LYP.

Thymine Bond Angles ° by DFT/B3LYP					
Angle	Exp ^b	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
C6-N1-C2	121.3	123.5258	123.6404	123.767	123.7725
N1-C6-C5	123.7	122.9099	122.617	122.7333	122.7066
C6-C5-Me	122.9	124.3419	123.6009	123.9131	123.8787
C4-C5-C6	118	118.7176	118.1356	117.946	117.9352
Me-C5-C4	119	116.9405	118.2634	118.1409	118.1861
C5-C4-O4	124.9	125.3035	125.134	125.0523	125.0611
C5-C4-N3	115.2	114.0675	114.9686	114.8371	114.8643
O4-C4-N3	119.9	120.629	119.8974	120.1105	120.0747
C4-N3-C2	127.2	128.5664	127.8062	127.9198	127.886
N1-C2-N3	114.6	112.2128	112.8321	112.7967	112.8355
N1-C2-O2	123.1	123.2733	123.0565	123.1272	123.1371
N3-C2-O2	122.3	124.5139	124.1113	124.076	124.0274
MAEP%		1.08	0.66	0.71	0.7

Exp^b: ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004)

In general using DFT/B3LYP method and using four basis sets (3-21G, 6-31G, 6-31G++dp, and aug-cc-pVDZ) gave a sufficient agreement with the experimental results for Pyrimidine and its derivatives in DNA nucleobases with error range from 0.32% to 1.39% of MAEP% for bond lengths and error range from 0.3% to 1.49% of MAEP% for bond angles.

5.1.2 Energy Analysis

5.1.2.1 Total Energy

Ground state energy of molecular system as mentioned above (2.3.2) is the sum of electron-electron repulsion energy, the kinetic energy of non-interacting system, exchange-correlation energy and external potential. In this study DFT was used and the exchange-correlation energy functional was the hybrid functional B3LYP, so the calculated energy may called E (B3LYP).

The energy analysis showed a decreasing in energy by increasing the basis sets (Table 5.11). That mean the lowest energies were by using (aug-cc-pVDZ) basis set (big basis set) since the energies were -264.3565, -467.3895, -542.639, -394.9961, and -454.2067 eV for Pyrimidine, Adenine, Guanine, Cytosine, and Thymine respectively. On the other hand the highest energies were obtained by using the smallest basis set (3-21G) since the total energies were -262.8511, -464.7214, -539.5421, -392.7439, and -451.6317 eV for Pyrimidine, Adenine, Guanine, Cytosine, and Thymine respectively.

Table 5.11. Total Energy E (B3LYP) eV for Pyrimidine and its derivatives in DNA Nucleobases.

Total Energy E (B3LYP) eV for Pyrimidine and its derivatives in DNA Nucleobases.				
DFT/B3LYP	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
Pyrimidine	-262.8511	-264.2337	-264.3409	-264.3565
Adenine	-464.7214	-467.1598	-467.3533	-467.3895
Guanine	-539.5421	-542.3698	-542.5917	-542.639
Cytosine	-392.7439	-394.8061	-394.9633	-394.9961
Thymine	-451.6317	-453.9961	-454.1703	-454.2067

5.1.2.2 Dipole Moment

In this study the dipole moment calculated using DFT/B3LYP method level too and the basis sets used are the same above.

Calculated Dipole Moments and experimental Dipole Moments taken form Ref (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004), (Kulakowska, Geller,

Lesyng, & Wierzchowski, 1974) and (Bergmann & Weiler-Feilchenfeld, 1973) gathered together in (table 5.12). In Pyrimidine the 3-21G basis set result showed the highest accuracy with 2.34 Debye and 3.34% of error. For Adenine calculation the 6-31G basis set was the best in accuracy with 2.48 Debye and 0.63% of error. Also, for Guanine the 6-31G basis set showed a good accuracy with 7.2 Debye and 1.5% of error. Moreover, for Cytosine the 6-31G basis set showed the highest accuracy over all with 7.002 Debye and 0.04% of error. Finally, for Thymine the 3-21G basis set gave the lowest error with 4 Debye and 2.3% of error.

Generally, the error range of the calculated dipole moment using DFT/B3LYP method was big a little bet and it was between 0.04% and 15.12%. In addition aug-cc-pVDZ basis set showed very low accuracy.

Table 5.12. Dipole Moment (Debye) of (Pyrimidine, A, G, C and T) calculated using DFT/B3LYP level.

Dipole Moment (Debye) of (Pyrimidine, A, G, C and T) calculated using DFT/B3LYP level						
DFT/B3LYP		3-21G	6-31G	6-31G++dp	aug-cc-pVDZ	Exp
Pyrimidine	Dipole moment (Debye)	2.3460	2.6133	2.4737	2.3785	2.27 ^d
	%error	3.34%	15.12%	8.97%	4.77%	
Adenine	Dipole moment (Debye)	2.3297	2.4842	2.4570	2.3903	2.5 ^b
	%error	6.81%	0.63%	1.72%	4.38%	
Guanine	Dipole moment (Debye)	6.7468	7.2072	6.8086	6.6723	7.1 ^b
	%error	4.97%	1.50%	4.10%	6.02%	
Cytosine	Dipole moment (Debye)	6.1820	7.0028	6.8927	6.6857	7 ^b
	%error	11.68%	0.04%	1.53%	4.49%	
Thymine	Dipole moment (Debye)	4.0049	4.6228	4.6126	4.4833	4.1 ^c
	%error	2.31%	12.75%	12.50%	9.34%	

Exp^b: (Preuss, Schmidt, Seino, Furthmüller, & Bechstedt, 2004). Exp^c: (Kulakowska, Geller, Lesyng, & Wierzchowski, 1974). Exp^d: (Bergmann & Weiler-Feilchenfeld, 1973).

5.1.2.3 HOMO-LUMO

In this study the MOs calculated using DFT/B3LYP method and the same basis sets mentioned above. The calculated energies of HOMO and LUMO and experimental data of the band gap taken from ref (Pino, et al., 2016), (Kilina, et al., 2007) and (Yamada & Fukutome, 1968) are gathered in (Table 5.13).

By comparing the band gap with the experimental data, in Pyrimidine the closest value was 5.41 eV by using 6-31G basis set, while in Adenine (Figure 5.1) the best value was by using aug-cc-pVDZ basis set with 5.29 eV. Again, in Guanine (Figure 5.2) the aug-cc-pVDZ basis set was the best with 5.16 eV. Moreover, in Cytosine (Figure 5.3) and Thymine (Figure 5.4) the 6-31G basis set was the best with 5.21 eV and 5.31 eV for Cytosine and Thymine respectively.

Table 5.13. HOMO-LUMO for Pyrimidine and its derivatives in DNA Nucleobases by DFT/B3LYP Level.

HOMO-LUMO for Pyrimidine and its derivatives in DNA Nucleobases by DFT/B3LYP Level						
DFT/B3LYP	MO	3-21G	6-31G	6-31G++dp	aug-cc-Pvdz	Exp
Pyrimidine	HOMO	-6.6087	-6.7771	-7.2541	-7.2470	5 ^e
	LUMO	-1.1380	-1.3633	-1.5823	-1.6185	
	Band Gap	5.4707	5.4138	5.6718	5.6285	
Adenine	HOMO	-5.8264	-6.0810	-6.2966	-6.2944	4.63 ^f
	LUMO	-0.3935	-0.7137	-0.9418	-0.9951	
	Band Gap	5.4329	5.3673	5.3548	5.2993	
Guanine	HOMO	-5.4220	-5.7303	-6.0729	-6.0653	4.59 ^f
	LUMO	0.1461	-0.3004	-0.8770	-0.8966	
	Band Gap	5.5681	5.4299	5.1959	5.1687	
Cytosine	HOMO	-5.9042	-6.2049	-6.5961	-6.5970	4.70 ^f
	LUMO	-0.5518	-0.9948	-1.3110	-1.3575	
	Band Gap	5.3523	5.2100	5.2851	5.2394	
Thymine	HOMO	-6.3956	-6.6737	-6.9570	-6.9409	4.8 ^f
	LUMO	-0.9069	-1.3573	-1.5548	-1.5921	
	Band Gap	5.4887	5.3164	5.4021	5.3488	

Exp^e: (Pino, et al., 2016).

Exp^f: (Kilina, et al., 2007) and (Yamada & Fukutome, 1968).

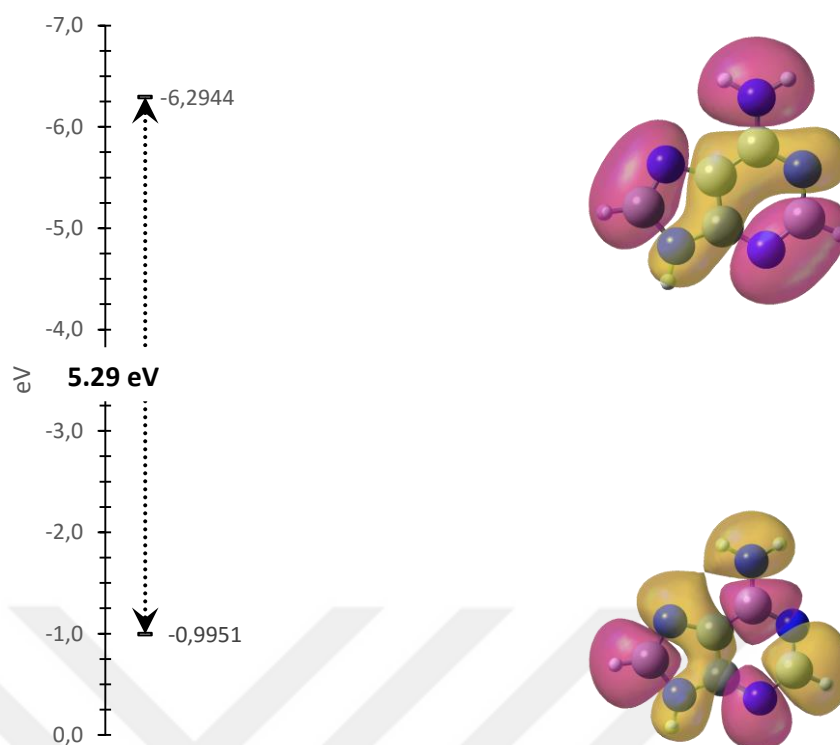


Figure 5.1. HOMO-LUMO and Band Gap for Adenine DFT/B3LYP aug-cc-pVDZ Basis set.

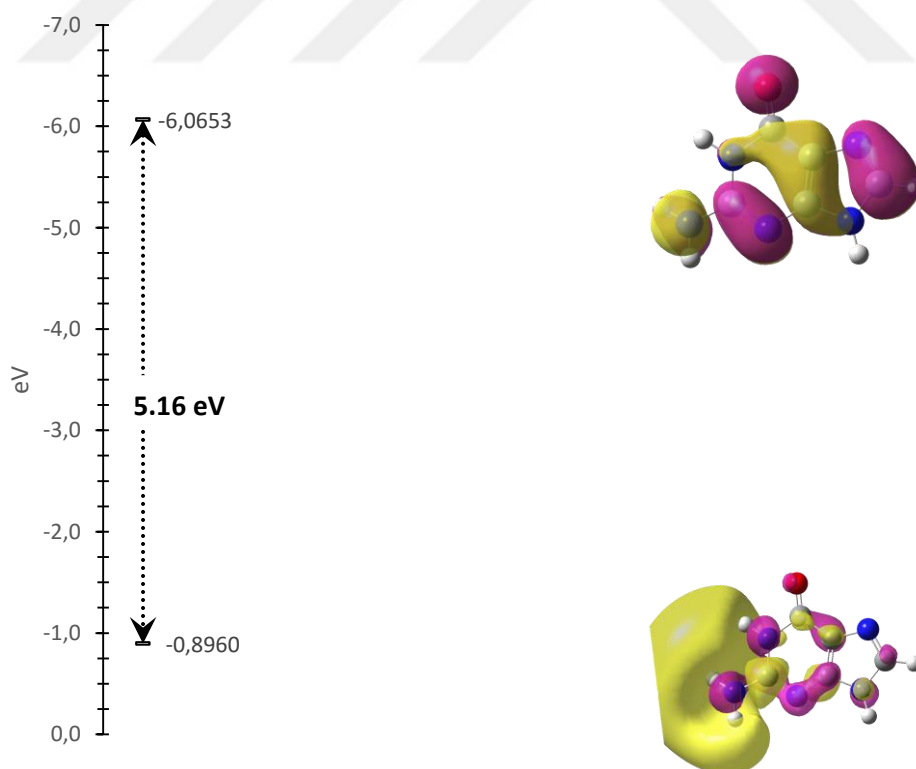


Figure 5.2. HOMO-LUMO and Band Gap for Guanine DFT/B3LYP aug-cc-pVDZ Basis set.

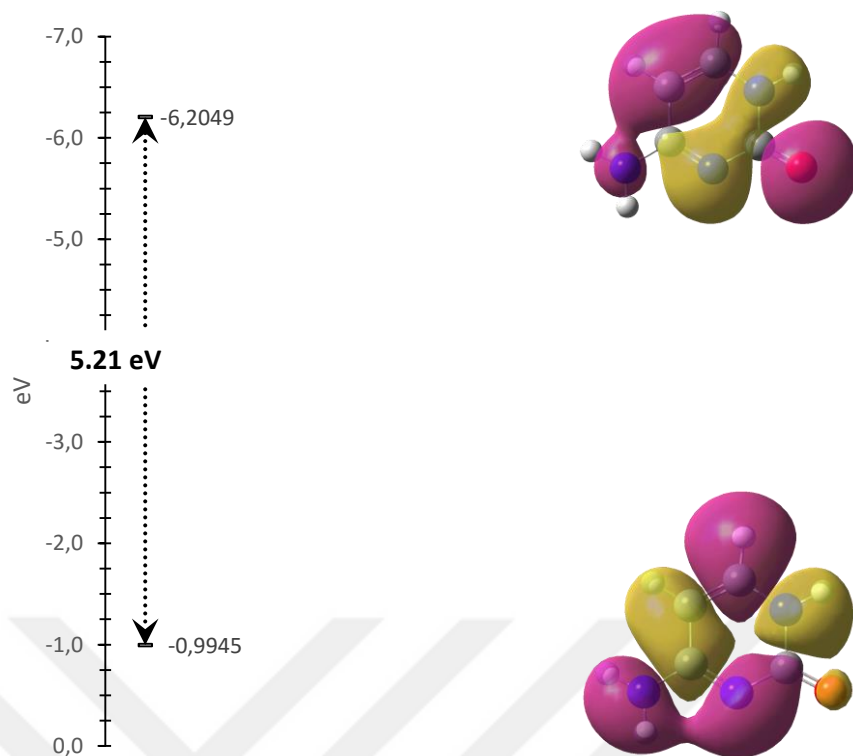


Figure 5.3. HOMO-LUMO and Band Gap for Cytosine DFT/B3LYP 6-31G Basis set.

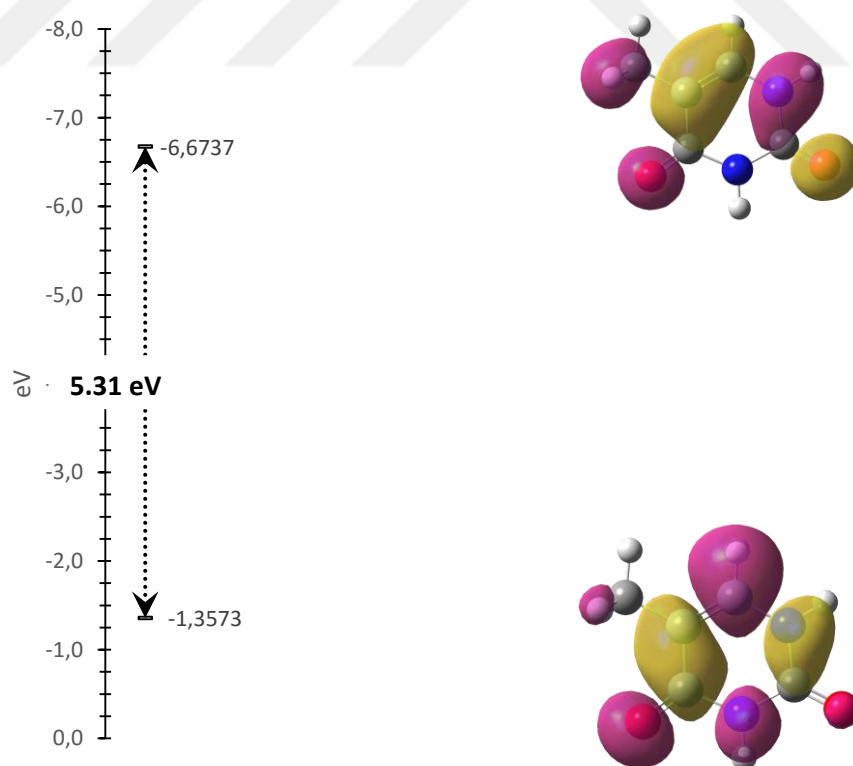


Figure 5.4. HOMO-LUMO and Band Gap for Thymine DFT/B3LYP 6-31G Basis set.

5.2 NOVEL COMPLEXES OF PLATINUM (II)

In this work the strategy of designing the complexes was by fixing both of the platinum (II) atom (the metal center) and the leaving groups (chlorine), and replacing the amine group by some of the DNA nucleobases specifically Adenine and Cytosine.

So, There are two complexes for platinum with adenine, the first complex designed by binding N1 of the Adenine to the Platinum (II) center as in (Figure 5.5) and will be mentioned as Complex A, the second complex designed by binding N7 of Adenine to the Platinum (II) center as in (Figure 5.6) and will be mentioned as Complex B. While the Cytosine has one complex with Platinum designed by binding N3 of the Cytosine to the metal center as in (Figure 5.7) and will be mentioned as Complex C.

All DNA nucleobases (Adenine and Cytosine) in the complexes are in cis position and the chlorine ligands are in cis position too, moreover, all complexes have a square planar geometry.

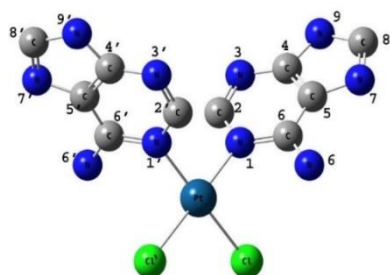


Figure 5.5. Complex A.

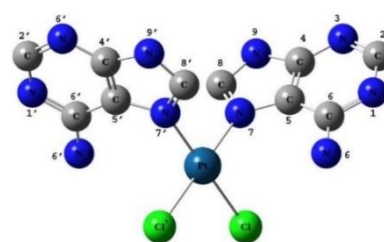


Figure 5.6. Complex B.

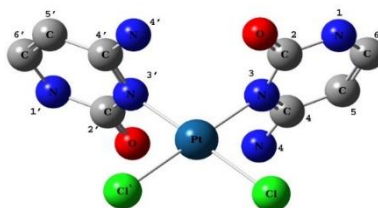


Figure 5.7. Complex C.

The calculations in this part of study have been done using DFT/B3LYP method level too and all frequencies calculations have positive value (no imaginary frequencis), see Appendix G.

The basis sets used in this study were (3-21G, 6-31G, 6-31G++dp, and 6-311G) basis sets for (Carbon, Chlorine, Nitrogen, Oxygen and Hydrogen) atoms. The basis sets used for platinum atom were Stuttgart/Dresden (SDD) basis set for outer shell electrons, and Los Alamos National Laboratory 2 (LANL2) basis set (effective core potentials) for the core electrons.

Notice: Since there is no experimental references for the designed complexes, so they will be compared with some cisplatin experimental values and will be discussed too.

5.2.1. Geometric Properties

The calculated geometric parameters (bond lengths and bond angles) of the designed novel complexes will be compared with the experimental geometric parameters of cisplatin Ref (Dodoff, 2012) (Raudaschl, et al., 1985).

The most important bonds are the bond that connecting the ligands to the metal center and that mean the Chlorine-Platinum bonds and Nitrogen-Platinum bonds. So, they will be compared to the experimental geometric parameters of cisplatin.

Consequently, for the bond lengths (Platinum-Nitrogen and Platinum-Chlorine) bonds will be discussed, and for bond angles (Nitrogen-Platinum-Nitrogen, Chlorine-Platinum-Nitrogen and Chlorine-Platinum-Chlorine) angles will be discussed too.

5.2.1.1 Bond Lengths

The calculated bond lengths for A, B and C Complexes are showed in (Tables 5.14, 5.15, 5.16) respectively.

Table 5.14. Bond Lengths for complex A By DFT/B3LYP level.

Bond Lengths for complex A By DFT/B3LYP level.				
Bonds	3-21G	6-31G	6-31G++dp	6-311G
Pt-Cl'	2.3928	2.3874	2.3873	2.39
Pt-Cl	2.39	2.3873	2.3873	2.39
Pt-N1	2.0601	2.0758	2.0758	2.0777
Pt-N1'	2.0639	2.0758	2.0758	2.0777
N1-C6	1.374	1.375	1.375	1.3753
N1-C2	1.3773	1.3751	1.3751	1.3744
C6-C5	1.4076	1.4115	1.4115	1.4093
C6-N6	1.3371	1.3416	1.3416	1.3407
C2-H	1.0794	1.0795	1.0795	1.0759
C2-N3	1.3289	1.3323	1.3323	1.3312
C5-N7	1.3945	1.3948	1.3948	1.3957
C5-C4	1.3974	1.3984	1.3984	1.394
N6-Ha	1.0208	1.0138	1.0138	1.0105
N6-Hb	1.0163	1.0092	1.0092	1.0064
N3-C4	1.3506	1.3541	1.3541	1.3549
N7-C8	1.326	1.3267	1.3267	1.3254
C4-N9	1.379	1.3793	1.3793	1.3788
C8-N9	1.3988	1.393	1.393	1.391
C8-H	1.0757	1.0771	1.0771	1.0739
N9-H	1.0133	1.0079	1.0079	1.0051
N1'-C6'	1.3749	1.375	1.375	1.3753
N1'-C2'	1.378	1.3751	1.3751	1.3744
C6'-C5'	1.4083	1.4115	1.4115	1.4093
C6'-N6'	1.3365	1.3416	1.3416	1.3407
C2'-H	1.0794	1.0795	1.0795	1.0759
C2'-N3'	1.3288	1.3323	1.3323	1.3312
C5'-N7'	1.3945	1.3948	1.3948	1.3957
C5'-C4'	1.3969	1.3984	1.3984	1.394
N6'-Ha	1.0214	1.0138	1.0138	1.0105
N6'-Hb	1.0164	1.0092	1.0092	1.0064
N3'-C4'	1.3507	1.3541	1.3541	1.3549
N7'-C8'	1.326	1.3267	1.3267	1.3254
C4'-N9'	1.3791	1.3793	1.3793	1.3788
C8'-N9'	1.3988	1.393	1.393	1.391
C8'-H	1.0757	1.0771	1.0771	1.0739
N9'-H	1.0133	1.0079	1.0079	1.0051

Table 5.15. Bond Lengths for complex B By DFT/B3LYP level.

Bond Lengths for complex B By DFT/B3LYP level				
Bonds	3-21G	6-31G	6-31G++dp	6-311G
Pt-Cl	2.3818	2.3812	2.3812	2.3837
Pt-Cl'	2.3818	2.3812	2.3812	2.3837
Pt-N7	2.0441	2.0525	2.0525	2.0535
Pt-N7'	2.0441	2.0525	2.0525	2.0535
N7-C8	1.3358	1.3332	1.3332	1.3315
N7-C5	1.4012	1.4032	1.4032	1.4046
C8-H	1.0747	1.0755	1.0755	1.0725
C8-N9	1.374	1.3723	1.3723	1.3706
C5-C6	1.4147	1.4192	1.4192	1.4173
C5-C4	1.4004	1.4029	1.4029	1.3995
N9-C4	1.3911	1.3878	1.3878	1.3869
N9-H	1.0133	1.0079	1.0079	1.0052
C6-N6	1.3459	1.3487	1.3487	1.348
C6-N1	1.3585	1.3629	1.3629	1.3637
C4-N3	1.339	1.345	1.345	1.3452
N6-Ha	1.0157	1.0091	1.0091	1.0062
N6-Hb	1.0198	1.0134	1.0134	1.0102
N1-C2	1.3476	1.3503	1.3503	1.3494
N3-C2	1.3529	1.3521	1.3521	1.3514
C2-H	1.0816	1.0821	1.0821	1.0778
N7'-C8'	1.3358	1.3332	1.3332	1.3315
N7'-C5'	1.4012	1.4032	1.4032	1.4046
C8'-H	1.0747	1.0755	1.0755	1.0725
C8'-N9'	1.374	1.3723	1.3723	1.3706
C5'-C6'	1.4147	1.4192	1.4192	1.4173
C5'-C4'	1.4004	1.4029	1.4029	1.3995
N9'-C4'	1.3911	1.3878	1.3878	1.3869
N9'-H	1.0133	1.0079	1.0079	1.0052
C6'-N6'	1.3459	1.3487	1.3487	1.348
C6'-N1'	1.3585	1.3629	1.3629	1.3637
C4'-N3'	1.339	1.345	1.345	1.3452
N6'-Ha'	1.0157	1.0091	1.0091	1.0062
N6'-Hb'	1.0198	1.0134	1.0134	1.0102
N1'-C2'	1.3476	1.3503	1.3503	1.3494
N3'-C2'	1.3529	1.3521	1.3521	1.3514
C2'-H	1.0816	1.0821	1.0821	1.0778

Table 5.16. Bond Lengths for complex C by DFT/B3LYP level.

Bond Lengths for complex C by DFT/B3LYP level				
Bonds	3-21G	6-31G	6-31G++dp	6-311G
Pt-Cl'	2.3885	2.388	2.3881	2.3908
Pt-Cl	2.3884	2.388	2.3881	2.3908
Pt-N3	2.0531	2.0684	2.0685	2.0693
Pt-N3'	2.0531	2.0685	2.0685	2.0693
N3-C4	1.3566	1.3602	1.3602	1.3605
N3-C2	1.3866	1.3865	1.3865	1.3862
C4-C5	1.4387	1.4395	1.4395	1.4383
C4-N4	1.3333	1.3375	1.3375	1.336
C2-N1	1.407	1.4049	1.4049	1.4023
C2-O	1.2451	1.2508	1.2508	1.2497
C5-C6	1.3547	1.3594	1.3594	1.3555
C5-H	1.0789	1.0806	1.0806	1.0773
N4-Ha	1.036	1.0249	1.0249	1.0213
N4-Hb	1.0139	1.0075	1.0075	1.0047
N1-C6	1.3685	1.3694	1.3694	1.3688
N1-H	1.0161	1.0104	1.0104	1.0075
C6-H	1.0813	1.0819	1.0819	1.0788
N3'-C4'	1.3566	1.3602	1.3602	1.3604
N3'-C2'	1.3866	1.3865	1.3865	1.3862
C4'-C5'	1.4387	1.4395	1.4395	1.4383
C4'-N4'	1.3333	1.3375	1.3375	1.336
C2'-N1'	1.407	1.4049	1.4049	1.4024
C2'-O	1.2451	1.2508	1.2508	1.2497
C5'-C6'	1.3547	1.3594	1.3594	1.3555
C5'-H	1.0789	1.0806	1.0806	1.0773
N4'-Ha	1.036	1.0249	1.0249	1.0213
N4'-Hb	1.0139	1.0075	1.0075	1.0047
N1'-C6'	1.3685	1.3694	1.3694	1.3688
N1'-H	1.0161	1.0104	1.0104	1.0075
C6'-H	1.0813	1.0819	1.0819	1.0788

5.2.1.1.1 Bond Lengths of Complexes A and B

By comparing the calculated bond lengths with cisplatin bond lengths for Complex B (Table 5.18) the Platinum-Chlorine bond length was closest to cisplatin in Complex B with (6-31G and 6-31G++dp) basis sets with 2.3812Å value.

Moreover, Platinum-Nitrogen bond lengths were closer in value to cisplatin in Complex B than Complex A, since 6-311G basis set gave the closest value to cisplatin with 2.0535Å.

On the other hand, by comparing the calculated bond lengths with cisplatin bond lengths for Complex A (Table 5.17) the Platinum-Chlorine bond length was closest to cisplatin by (6-31G and 6-31G++dp) basis sets with 2.3873Å.

Moreover, the closest Platinum-Nitrogen bond lengths were 2.0601Å and 2.0639Å for Pt-N1 and Pt-N1' respectively by 3-21G basis set.

Table 5.17. Comparing the calculated bond lengths with cisplatin bond lengths (complex A).

Comparing the calculated bond lengths with cisplatin bond lengths (complex A)					
Bonds	3-21G	6-31G	6-31G++dp	6-311G	Exp ^g
Pt-Cl'	2.3928	2.3874	2.3873	2.39	2.318
Pt-Cl	2.39	2.3873	2.3873	2.39	2.318
Pt-N1	2.0601	2.0758	2.0758	2.0777	2.054
Pt-N1'	2.0639	2.0758	2.0758	2.0777	2.054

Exp^g: (Dodoff, 2012) (Raudaschl, et al., 1985).

Table 5.18. Comparing the calculated bond lengths with cisplatin bond lengths (complex B).

Comparing the calculated bond lengths with cisplatin bond lengths (complex B)					
Bonds	3-21G	6-31G	6-31G++dp	6-311G	Exp ^g
Pt-Cl'	2.3818	2.3812	2.3812	2.3837	2.318
Pt-Cl	2.3818	2.3812	2.3812	2.3837	2.318
Pt-N7	2.0441	2.0525	2.0525	2.0535	2.054
Pt-N7'	2.0441	2.0525	2.0525	2.0535	2.054

Exp^g: (Dodoff, 2012) (Raudaschl, et al., 1985).

5.2.1.1.2 Bond Lengths of Complex C

By comparing the calculated bond lengths with cisplatin bond lengths (Table 5.19) the Platinum-Chlorine bond length was closest to cisplatin by using 6-31G and 6-31G++dp basis sets with 2.3881Å.

On the other hand, Platinum-Nitrogen bond lengths was closet in value to cisplatin by 3-21G basis set with 2.0531Å.

Table 5.19. Comparing the calculated bond lengths with cisplatin bond lengths (complex C).

Comparing the calculated bond lengths with cisplatin bond lengths (complex C)					
Bonds	3-21G	6-31G	6-31G++dp	6-311G	Exp ^g
Pt-Cl'	2.3885	2.388	2.3881	2.3908	2.318
Pt-Cl	2.3884	2.388	2.3881	2.3908	2.318
Pt-N1	2.0531	2.0684	2.0685	2.0693	2.054
Pt-N1'	2.0531	2.0685	2.0685	2.0693	2.054

Exp^g: (Dodoff, 2012) (Raudaschl, et al., 1985).

In general the bond lengths of the designed complexes gave a good result comparing to the bond lengths of cisplatin.

5.2.1.2 Bond Angles

The calculated bond angles for A, B and C complexes are showed in (Tables 5.20, 5.21 and 5.22) respectively.

Table 5.20. Bond Angles for complex A by DFT/B3LYP level.

Bond Angles for complex A by DFT/B3LYP level				
Angles	3-21G	6-31G	6-31G++dp	6-311G
Cl-Pt-Cl'	91.58	91.81	91.81	91.49
Cl'-Pt-N1'	89.66	88.93	88.93	89.11
Cl-Pt-N1	88.95	88.92	88.93	89.11
N1-Pt-N1'	89.81	90.33	90.33	90.28
Pt-N1-C6	120.99	121.39	121.40	121.44
Pt-N1-C2	118.82	118.51	118.51	118.48
C6-N1-C2	120.18	120.09	120.09	120.07
N1-C6-C5	116.33	116.39	116.39	116.30
N1-C6-N6	121.16	121.05	121.05	121.13
C5-C6-N6	122.50	122.56	122.56	122.56
N1-C2-H	115.12	115.46	115.46	115.53
N1-C2-N3	126.15	126.49	126.49	126.46
H-C2-N3	118.73	118.05	118.05	118.00
C6-C5-N7	130.49	130.72	130.72	130.54
C6-C5-C4	118.38	118.28	118.28	118.46

Table 5.20. Bond Angles for complex A by DFT/B3LYP level (Continued).

Bond Angles for complex A by DFT/B3LYP level				
Angles	3-21G	6-31G	6-31G++dp	6-311G
N7-C5-C4	111.13	111.00	111.00	110.99
C6-N6-Ha	119.05	119.38	119.38	119.68
C6-N6-Hb	118.36	118.84	118.84	118.84
Ha-N6-Hb	119.95	119.72	119.72	119.49
C2-N3-C4	113.43	113.11	113.11	113.09
C4-N7-C8	104.56	104.48	104.48	104.46
C5-C4-N3	125.51	125.62	125.62	125.58
C5-C4-N9	105.20	105.20	105.20	105.24
N3-C4-N9	129.29	129.18	129.18	129.17
N7-C8-N9	112.20	112.38	112.38	112.33
N7-C8-H	125.68	125.27	125.27	125.16
N9-C8-H	122.13	122.35	122.35	122.51
C4-N9-C8	106.91	106.94	106.94	106.97
C4-N9-H	125.42	125.60	125.60	125.41
C8-N9-H	127.66	127.45	127.45	127.61
Pt-N1'-C6'	121.53	121.40	121.40	121.44
Pt-N1'-C2'	118.41	118.51	118.50	118.48
C6'-N1'-C2'	120.06	120.09	120.09	120.07
N1'-C6'-C5'	116.30	116.38	116.39	116.30
N1'-C6'-N6'	121.39	121.05	121.05	121.13
C5'-C6'-N6'	122.30	122.56	122.56	122.56
N1'-C2'-H	115.10	115.46	115.46	115.53
N1'-C2'-N3'	126.27	126.49	126.49	126.46
H-C2'-N3'	118.63	118.05	118.05	118.00
C6'-C5'-N7'	130.39	130.71	130.72	130.54
C6'-C5'-C4'	118.48	118.28	118.28	118.46
N7-C5-C4	111.13	111.00	111.00	110.99
C6'-N6'-Ha'	119.10	119.38	119.38	119.68
C6'-N6'-Hb'	118.16	118.84	118.84	118.84
Ha'-N6'-Hb'	119.83	119.72	119.72	119.49
C2'-N3'-C4'	113.41	113.11	113.11	113.09
C4'-N7'-C8'	104.57	104.48	104.48	104.46
C5'-C4'-N3'	125.46	125.62	125.62	125.58
C5'-C4'-N9'	105.22	105.20	105.20	105.24
N3'-C4'-N9'	129.32	129.18	129.18	129.17
N7'-C8'-N9'	112.19	112.38	112.38	112.33
N7'-C8'-H	125.69	125.27	125.27	125.16
N9'-C8'-H	122.13	122.35	122.35	122.51
C4'-N9'-C8'	106.90	106.94	106.94	106.97
C4'-N9'-H	125.43	125.60	125.60	125.41
C8'-N9'-H	127.66	127.45	127.45	127.61

Table 5.21. Bond Angles for complex B by DFT/B3LYP level.

Bond Angles for complex B by DFT/B3LYP level				
Angles	3-21G	6-31G	6-31G++dp	6-311G
Cl'-Pt-Cl	92.36	92.32	92.32	92.09
Cl'-Pt-N7'	87.69	88.00	88.00	88.17
Cl'-Pt-N7	87.69	88.00	88.00	88.16
N7'-Pt-N7	92.32	91.68	91.68	91.59

Table 5.21. Bond Angles for complex B by DFT/B3LYP level (Continued).

Bond Angles for complex B by DFT/B3LYP level				
Angles	3-21G	6-31G	6-31G++dp	6-311G
Pt-N7-C8	127.04	125.81	125.81	125.82
Pt-N7-C5	125.81	127.27	127.27	127.35
C8-N7-C5	107.11	106.91	106.91	106.82
N9-C8-H	125.14	125.03	125.03	124.94
N7-C8-N9	110.31	110.68	110.69	110.74
H-C8-N9	124.55	124.28	124.28	124.31
N7-C5-C6	134.20	134.66	134.66	134.60
N7-C5-C4	108.56	108.41	108.40	108.39
C6-C5-C4	117.24	116.94	116.94	117.01
C8-N9-C4	108.26	108.12	108.12	108.10
C8-N9-H	126.88	126.86	126.86	127.12
C4-N9-H	124.85	125.00	125.00	124.78
C5-C6-N6	124.18	124.50	124.50	124.70
C5-C6-N1	117.26	117.30	117.30	117.18
N6-C6-N1	118.56	118.20	118.20	118.12
C5-C4-N9	105.75	105.87	105.87	105.94
C5-C4-N3	126.21	126.46	126.46	126.50
N9-C4-N3	128.04	127.67	127.67	127.56
C6-N6-Ha	117.30	117.54	117.54	117.49
C6-N6-Hb	120.70	120.91	120.91	121.07
Ha-N6-Hb	119.69	119.50	119.50	119.32
C6-N1-C2	119.87	119.92	119.92	120.05
C4-N3-C2	112.15	112.04	112.04	112.08
N1-C2-N3	127.24	127.30	127.30	127.11
N1-C2-H	116.36	116.17	116.17	116.24
N3-C2-H	116.39	116.53	116.53	116.65
Pt-N7'-C8'	127.04	125.80	125.81	125.81
Pt-N7'-C5'	125.81	127.28	127.27	127.35
C8'-N7'-C5'	107.11	106.91	106.91	106.82
N9-C8-H	125.14	125.03	125.03	124.94
N7'-C8'-N9'	110.31	110.69	110.69	110.74
H-C8'-N9'	124.55	124.28	124.28	124.31
N7'-C5'-C6'	134.20	134.66	134.66	134.60
N7'-C5'-C4'	108.56	108.40	108.40	108.39
C6'-C5'-C4'	117.24	116.94	116.94	117.01
C8'-N9'-C4'	108.26	108.12	108.12	108.10
C8'-N9'-H	126.88	126.86	126.86	127.12
C4'-N9'-H	124.85	125.00	125.00	124.78
C5'-C6'-N6'	124.18	124.50	124.50	124.71
C5'-C6'-N1'	117.26	117.30	117.30	117.18
N6'-C6'-N1'	118.56	118.20	118.20	118.11
C5'-C4'-N9'	105.75	105.87	105.87	105.94
C5'-C4'-N3'	126.21	126.46	126.46	126.50
N9'-C4'-N3'	128.04	127.67	127.67	127.55
C6'-N6'-Ha'	117.30	117.54	117.54	117.49
C6'-N6'-Hb'	120.70	120.91	120.91	121.07
Ha'-N6'-Hb'	119.69	119.50	119.50	119.32
C6'-N1'-C2'	119.87	119.92	119.92	120.06
C4'-N3'-C2'	112.15	112.04	112.04	112.08
N1'-C2'-N3'	127.24	127.30	127.30	127.11
N1'-C2'-H	116.36	116.17	116.17	116.24
N3'-C2'-H	116.39	116.53	116.53	116.65

Table 5.22. Bond Angles for complex C by DFT/B3LYP level.

Bond Angles for complex C by DFT/B3LYP level				
Angles	3-21G	6-31G	6-31G++dp	6-311G
Cl'-Pt-Cl	93.4522	92.9987	92.9972	92.7611
Cl'-Pt-N3'	85.7481	85.8964	85.8956	86.0609
Cl-Pt-N3	85.7512	85.8993	85.8999	86.0623
N3-Pt-N3'	95.055	95.2183	95.2199	95.1277
Pt-N3-C4	120.6294	120.7615	120.7599	120.8889
Pt-N3-C2	115.0532	116.3657	116.3672	116.4912
C4-N3-C2	122.8614	121.8338	121.8349	121.7405
N3-C4-C5	119.5474	120.2083	120.2079	120.1367
N3-C4-N4	118.5688	118.5389	118.5344	118.5698
N5-C4-N4	121.8826	121.2508	121.2557	121.2927
N3-C2-N1	115.3853	116.0277	116.0272	116.0197
N3-C2-O	124.0282	124.2181	124.2194	124.2206
N1-C2-O	120.5852	119.7514	119.7507	119.757
C4-C5-C6	118.0949	118.1576	118.1577	118.2435
C4-C5-H	120.5401	120.4689	120.4686	120.461
C6-C5-H	121.3512	121.367	121.3672	121.2885
C4-N4-Ha	120.2538	120.1894	120.1882	120.3052
C4-N4-Hb	120.7311	120.9689	120.9688	121.0577
Ha-N4-Hb	118.9936	118.8143	118.8152	118.5634
C2-N1-C6	122.8288	123.2155	123.2153	123.2374
C2-N1-H	115.7543	115.2191	115.2178	115.2517
C6-N1-H	121.3888	121.5488	121.5503	121.503
C5-C6-N1	120.7594	120.0987	120.0988	120.1028
C5-C6-H	122.4274	123.0958	123.0949	123.1674
N1-C6-H	116.8055	116.8004	116.8011	116.7253
Pt-N3'-C4'	120.6251	120.7609	120.7592	120.8904
Pt-N3'-C2'	115.0579	116.3661	116.3646	116.4865
C4'-N3'-C2'	122.8608	121.835	121.8366	121.743
N3'-C4'-C5'	119.5485	120.2084	120.2077	120.136
N3'-C4'-N4'	118.5645	118.5359	118.5343	118.5706
N5'-C4'-N4'	121.8858	121.2537	121.256	121.2925
N3'-C2'-N1'	115.387	116.0274	116.0263	116.017
N3'-C2'-O	124.0266	124.2187	124.2183	124.2205
N1'-C2'-O	120.585	119.7506	119.7524	119.7597
C4'-C5'-C6'	118.0947	118.1572	118.1572	118.2434
C4'-C5'-H	120.5389	120.469	120.4688	120.4611
C6'-C5'-H	121.3525	121.3675	121.3676	121.2885
C4'-N4'-Ha'	120.2603	120.1907	120.1906	120.3108
C4'-N4'-Hb'	120.7268	120.9686	120.9675	121.0536
Ha'-N4'-Hb'	118.9918	118.8136	118.8145	118.5622
C2'-N1'-C6'	122.8295	123.2157	123.2158	123.2379
C2'-N1'-H	115.755	115.2189	115.2189	115.2513
C6-N1-H	121.3874	121.5486	121.5485	121.5029
C5'-C6'-N1'	120.7579	120.099	120.0989	120.1037
C5'-C6'-H	122.4304	123.0956	123.0956	123.1666
N1'-C6'-H	116.8041	116.8002	116.8002	116.7251

5.2.1.2.1 Bond Angles of Complexes A and B

By comparing the angles of the designed complexes (A and B) with the angles of cisplatin Shown in (Tables 5.23 and 5.24) respectively, the Nitrogen-Platinum-Nitrogen angle was closest in value in Complex A (N1-Pt-N1') by using 6-311G basis set with 90.28 degrees, and was 91.68 degrees by 6-31G and 6-31G++dp in Complex B (N7-Pt-N7').

For the Chlorine-Platinum-Nitrogen angle the Complex A gave a good value by using 6-31G and 6-31G++dp basis sets since the angle (Cl-Pt-N1 and Cl'-Pt-N1') was 88.93 degrees.

On the other hand, the results of Complex B were closest by using 6-311G basis set with 8.17 degrees for (Cl-Pt-N7 and Cl'-Pt-N7') angles.

Moreover, the Chlorine-Platinum-Chlorine angle was closest in value for the Complex A since it was 91.81 degrees for (Cl-Pt-Cl') angle by using 6-31G and 6-31G++dp basis sets, on the other hand the closest value was 92.09 degrees (Cl-Pt-Cl') angle by using 6-311G basis set for the Complex B.

Table 5.23. Comparing the calculated bond Angles with cisplatin bond Angles (complex A).

Comparing the calculated bond Angles with cisplatin bond Angles (complex A)					
Angles	3-21G	6-31G	6-31G++dp	6-311G	Exp ^g
N1-Pt-N1'	89.81	90.33	90.33	90.28	90.2
Cl'-Pt-N1'	89.66	88.93	88.93	89.11	88.9
Cl-Pt-N1	88.95	88.92	88.93	89.11	88.9
Cl-Pt-Cl'	91.58	91.81	91.81	91.49	91.9

Exp^g: (Dodoff, 2012) (Raudaschl, et al., 1985).

Table 5.24. Comparing the calculated bond Angles with cisplatin bond Angles (complex B).

Comparing the calculated bond Angles with cisplatin bond Angles (complex B)					
Angles	3-21G	6-31G	6-31G++dp	6-311G	Exp ^g
N7'-Pt-N7	92.32	91.68	91.68	91.59	90.2
Cl'-Pt-N7'	87.69	88.00	88.00	88.17	88.9
Cl'-Pt-N7	87.69	88.00	88.00	88.16	88.9
Cl'-Pt-Cl	92.36	92.32	92.32	92.09	91.9

Exp^g: (Dodoff, 2012) (Raudaschl, et al., 1985).

5.2.1.2.2 Bond Angles of Complex C

The best angles between the ligands in the square planar geometry is 90 degrees. But in this complex the values were little bet crude than 90 degrees for Nitrogen-Platinum-Nitrogen angle and for Chlorine-Platinum-Nitrogen angles and this steric distortion caused by the repulsion between the nitrogen atoms and oxygen atoms.

By comparing the angles of the Complex C with the angles of cisplatin gathered in (Table 5.25) the Nitrogen-Platinum-Nitrogen angle was 95.055, 95.2183, 95.2199, and 95.2177 degrees by using 3-21G, 6-31G, 6-31G++dp, and 6-311G respectively.

While the Chlorine-Platinum-Nitrogen angles were less crude than the Nitrogen-Platinum-Nitrogen angle since the closest value was 86.0623 degrees (Cl-Pt-N3') by using 6-311G basis set, and the most crude value was 85.7481 degrees (Cl'-Pt-N3') by using 3-21G basis set.

On the other hand the Chlorine-Platinum- Chlorine angle was normal compared to the last angles and the closest value was 92.7611 degrees by using 6-311G basis set.

Table 5.25. Comparing the calculated bond Angles with cisplatin bond Angles (complex C).

Comparing the calculated bond Angles with cisplatin bond Angles (complex C)					
Angles	3-21G	6-31G	6-31G++dp	6-311G	Exp ^g
Cl'-Pt-Cl	93.4522	92.9987	92.9972	92.7611	91.9
Cl'-Pt-N3'	85.7481	85.8964	85.8956	86.0609	88.9
Cl-Pt-N3	85.7512	85.8993	85.8999	86.0623	88.9
N3-Pt-N3'	95.055	95.2183	95.2199	95.1277	90.2

Exp^g: (Dodoff, 2012) (Raudaschl, et al., 1985).

5.2.1.3 Dihedrals

The results of dihedrals calculation show that the Complexes A and B (Table 5.26) and (Table 5.27) respectively have a square planer geometry.

On the other hand, the dihedrals of the Complex C (Table 5.28) show that the geometry is also square planer but with some distortion caused by intramolecular interaction between Oxygen and Nitrogen atoms.

Table 5.26. Dihedrals values of complex A by DFT/B3LYP method.

Dihedrals values of complex A by DFT/B3LYP method				
Dihedrals	3-21G	6-31G	6-31G++dp	6-311G
Pt-N1-C6-C4	-179.022	-179.164	-179.145	-179.098
Pt-N1-C6-N6	0.0446	0.0597	0.0793	0.2204
Pt-N1-C2-N3	179.1607	179.4112	179.3964	179.3133
Pt-N1'-C6'-C4'	-177.201	-179.129	-179.139	-179.095
Pt-N1'-C6'-N6'	1.9523	0.0959	0.0857	0.2232
Pt-N1'-C2'-N3'	177.5011	179.3765	179.3901	179.3106

Table 5.27. Dihedrals values of complex B by DFT/B3LYP method.

Dihedrals values of complex B by DFT/B3LYP method				
Dihedrals	3-21G	6-31G	6-31G++dp	6-311G
Pt-N7-C8-N9	-178.593	-179.504	-179.498	-179.699
Pt-N7-C5-C6	-0.8078	0.1353	0.1298	0.5338
Pt-N7-C5-C4	178.8521	179.7492	179.7429	179.997
Pt-N7'-C8'-N9'	-178.596	-179.512	-179.507	-179.722
Pt-N7'-C5'-C6'	-0.8043	0.1425	0.1377	0.5517
Pt-N7'-C5'-C4'	178.8552	179.7575	179.7521	-179.986

Table 5.28. Dihedrals values of complex C by DFT/B3LYP method.

Dihedrals values of complex C by DFT/B3LYP method				
Dihedrals	3-21G	6-31G	6-31G++dp	6-311G
Pt-N3-C4-C5	-157.73	-160.438	-160.447	-160.905
Pt-N3-C4-N4	22.6663	20.069	20.0674	19.4273
Pt-N3-C2-N1	158.1968	160.8797	160.8863	161.2469
Pt-N3-C2-O	-22.2175	-19.7296	-19.7223	-19.3562
Pt-N3'-C4'-C5'	-157.736	-160.445	-160.44	-160.904
Pt-N3'-C4'-N4'	22.6544	20.0654	20.0672	19.4334
Pt-N3'-C2'-N1'	158.2051	160.902	160.89	161.2485
Pt-N3'-C2'-O	-22.2224	-19.7604	-19.7435	-19.367

5.2.2 Energy Analysis

5.2.2.1 Total Energy

By analyzing the total energy of the complexes, showed in (Table 5.29), the Complex C was in general the highest in energy with -1829.282 Hartrees by using 6-311-G basis set and witch is a big basis set.

On the other hand, the Adenine two complexes (A and B) were almost equal in energy with very small difference between 0.002 and 0.005 Hartrees and the lowest energy value was -1973.994 Hartree by using 6-311G too.

Table 5.29. Total energy (au) of the designed complexes (A, B and C) by DFT/B3LYP level.

Total energy (au) of the designed complexes (A, B and C) by DFT/B3LYP level				
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G
Complex A	-1964.515	-1973.710	-1973.710	-1973.994
Complex B	-1964.520	-1973.712	-1973.712	-1973.996
Complex C	-1820.595	-1829.020	-1829.020	-1829.282

5.2.2.2 Zero Point Energy (ZPE)

“The existence of a zero-point energy is probable” (Einstein and Stern 1913) (Milonni, 1994). The zero-point energy can be define as the lowest energy of a quantum mechanical system can have (Irikura, 2007)

The zero-point energies, gathered in (Table 5.30), are show that for adenine complexes zero-point energies were almost equal with deference between 0.028 and 0.141 (Kcal/Mol) since the highest zero-point energy was 146.848 (Kcal/Mol) by using 6-31G and 6-31G++dp basis sets for the Complex B and the lowest zero-point energy was 145.471 (Kcal/Mol) by using 3-21G basis set for Complex A.

On the other hand, the zero-point energy of Complex C was lower than the Adenine complexes since the higher value was 130.525 (Kcal/Mol) by using 6-31G and 6-31G++dp basis sets and the lowest value was 129.616 (Kcal/Mol) by using 6-311G basis set.

Table 5.30. Zero-point vibrational energy (Kcal/Mol) of the designed complexes (A, B and C) by DFT/B3LYP level.

ZPE (Kcal/Mol) of the designed complexes (A, B and C) by DFT/B3LYP level				
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G
Complex A	145.471	146.820	146.820	145.886
Complex B	145.612	146.848	146.848	145.857
Complex C	129.617	130.525	130.525	129.616

5.2.3 Dipole Moment

In general the highest dipole moment values, showed in (Table 5.31), were in Complex C since it was 16.023 Debye by 3-21G basis set. On the other hand the values were smallest in Complex B with 9.473 Debye by 6-31G and 6-31G++dp basis sets.

Moreover, the Complex A dipole moment values were near to the Complex C since the highest value was 14.188 Debye by 3-21G basis set and the smallest value was 13.770 by 6-31G basis set.

Table 5.31. Dipole Moment (Debye) of the designed complexes (A, B and C) by DFT/B3LYP level.

Dipole Moment (Debye) of the designed complexes (A, B and C) by DFT/B3LYP level				
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G
Complex A	14.188	13.770	13.771	13.958
Complex B	9.996	9.473	9.473	9.635
Complex C	16.023	15.693	15.692	15.954

5.2.4 HOMO-LUMO

The energies of HOMO-1, HOMO, LUMO, and LUMO+1 orbitals and the band gap energy between HOMO and LUMO orbitals for Complexes (A, B, and C) are gathered in (Table 5.32).

The high value of E_{HOMO} of a molecule indicates the probability of the tendency to donate electrons of this molecule to a suitable acceptor with low E_{LUMO} .

On the contrary the low value of the E_{LUMO} of a molecule indicates the probability of the tendency of this molecule to accept electrons from suitable donator with high E_{HOMO} .

Consequently, by taking the average of the E_{HOMO} values with several basis sets the order of tendency to donate electrons is Complex C > Complex A > Complex B, so Complex C expected to be the best donator of this three complexes.

On the other hand the average of tendency to accept electrons is Complex A > Complex B > Complex C.

The highest band gap of the HOMO-LUMO values were in Complex B since the values were 4.544, 4.417, 4.417, 4.404 eV by using 3-21G, 6-31G, 6-31G++dp 6-311G basis sets respectively. The lowest band gap of the HOMO-LUMO values were in Complex C since the values were 3.464, 3.429, 3.429, 3.421 eV by using 3-21G, 6-31G, 6-31G++dp 6-311G basis sets respectively.

On the other hand, in Complex A the values were closer to Complex B but almost smaller with 4.521, 4.379, 4.379 eV by using 3-21G, 6-31G, 6-31G++dp 6-311G basis sets respectively.

Table 5.32. HOMO-1, HOMO, LUMO, and LUMO+1 for complexes (A, B and C) by DFT/B3LYP level.

HOMO-1, HOMO, LUMO, and LUMO+1 for complexes (A, B and C) by DFT/B3LYP level							
Complex	MO		3-21G	6-31G	6-31G++dp	6-311G	Average
Complex A	LUMO+1 au		-0.050	-0.057	-0.057	-0.063	-0.057
	LUMO au		-0.050	-0.058	-0.058	-0.065	-0.058
	HOMO au		-0.216	-0.219	-0.219	-0.225	-0.220
	HOMO-1 au		-0.222	-0.224	-0.224	-0.230	-0.225
	HOMO-LUMO BAND Gap	au	0.166	0.161	0.161	0.162	0.162
		eV	4.521	4.379	4.379	4.412	4.412
Complex B	LUMO+1 au		-0.056	-0.064	-0.064	-0.070	-0.063
	LUMO au		-0.060	-0.068	-0.068	-0.074	-0.067
	HOMO au		-0.227	-0.230	-0.230	-0.236	-0.231
	HOMO-1 au		-0.232	-0.236	-0.236	-0.242	-0.236
	HOMO-LUMO BAND Gap	Au	0.167	0.162	0.162	0.162	0.163
		Ev	4.544	4.417	4.417	4.404	4.445

Table 5.32. HOMO-1, HOMO, LUMO, and LUMO+1 for complexes (A, B and C) by DFT/B3LYP level (Continued).

HOMO-1, HOMO, LUMO, and LUMO+1 for complexes (A, B and C) by DFT/B3LYP level							
Complex	MO		3-21G	6-31G	6-31G++dp	6-311G	Average
Complex C	LUMO+1 au		-0.059	-0.066	-0.066	-0.073	-0.066
	LUMO au		-0.063	-0.069	-0.069	-0.076	-0.069
	HOMO au		-0.190	-0.195	-0.195	-0.202	-0.196
	HOMO-1 au		-0.194	-0.200	-0.200	-0.207	-0.200
	HOMO-LUMO BAND Gap	au	0.127	0.126	0.126	0.126	0.126
		eV	3.464	3.429	3.429	3.421	3.436

In the HOMO - LUMO orbitals (Figure 5.8), HOMO electrons are localized mainly in the (Cl) leaving group of the complex, meanwhile, LUMO electrons are localized mainly over the ligand molecular part for all three complexes.

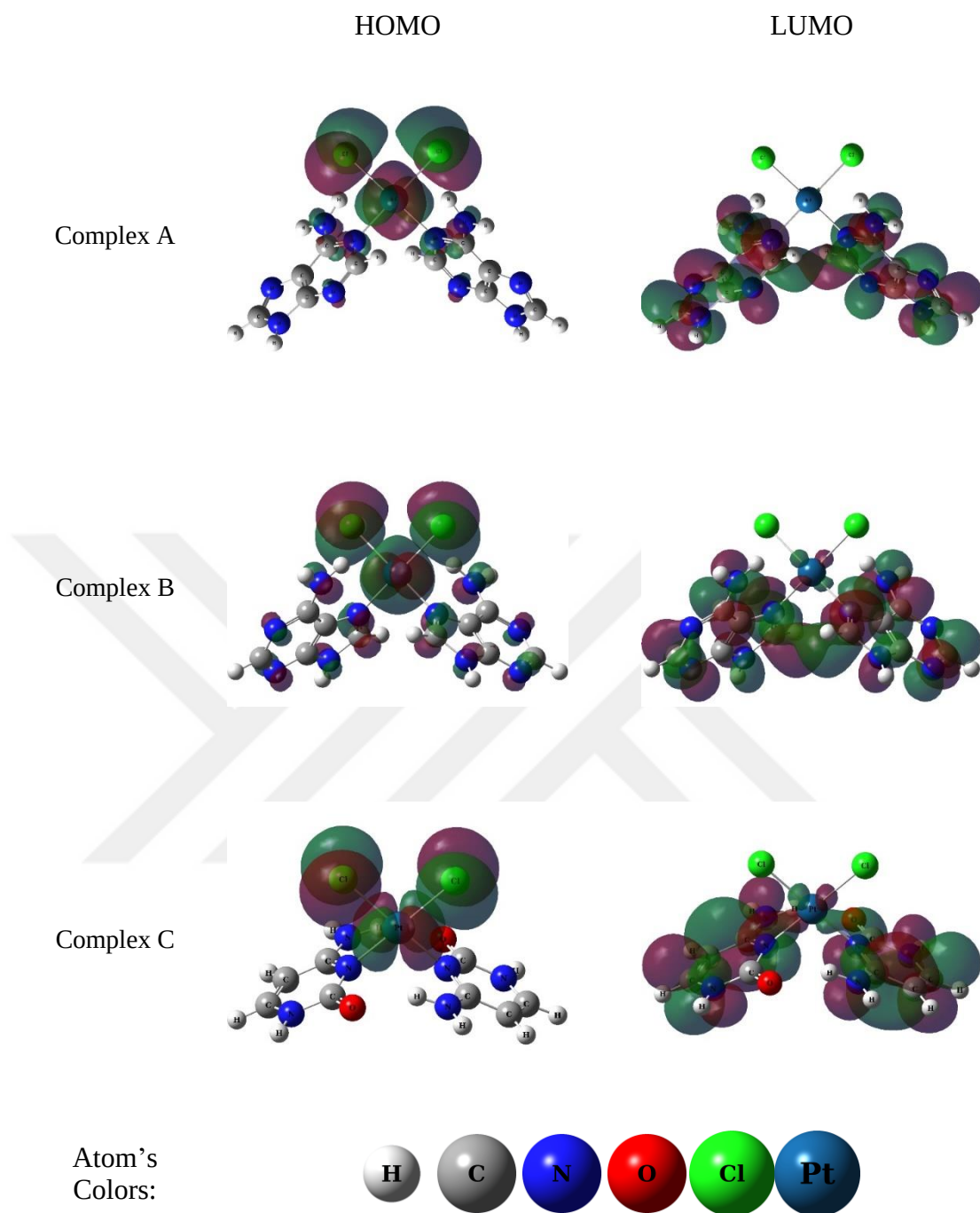


Figure 5.8. Molecular Orbitals Surface for HOMO and LUMO of (A, B and C) Complexes computed at DFT/B3LYP level and 6-311G basis set.

5.2.5 Chemical Properties

5.2.5.1 Ionization Potential (I)

(Table 5.33) shows the calculated ionization potential of the three complexes and the average of using several basis sets.

Small ionization energy indicates high reactivity of the molecules and high ionization energy indicates high stability and chemical inertness (Rajak, Islam, & Ghosh, 2011).

Consequently, the order of expected stability of the three complexes is Complex C > Complex A > Complex B. So Complex C expected to be the highest in stability, and Complex B expected to be the highest in reactivity.

Table 5.33. Ionization Potential (I) eV of the Complexes (A, B and C) By DFT/B3LYP level.

Ionization Potential (I) eV of the Complexes (A, B and C) By DFT/B3LYP level					
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G	Average
Complex A	5.891	5.957	5.957	6.125	5.982
Complex B	6.169	6.259	6.259	6.423	6.278
Complex C	5.178	5.313	5.313	5.495	5.325

5.2.5.2 Electron Affinity (A)

(Table 5.34) shows the calculated electron affinity of the three complexes and the average of using several basis sets.

The order of the electron affinity between the three complexes is Complex C > Complex B > Complex A.

Table 5.34. Electron Affinity (A) eV of the Complexes (A, B and C) By DFT/B3LYP level.

Electron Affinity (A) eV of the Complexes (A, B and C) By DFT/B3LYP level					
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G	Average
Complex A	1.370	1.578	1.578	1.757	1.571
Complex B	1.625	1.842	1.842	2.019	1.832
Complex C	1.715	1.885	1.885	2.074	1.890

5.2.5.3 Electronegativity (χ)

(Table 5.35) shows the calculated Electronegativity of the three complexes and the average of using several basis sets.

Generally, the electronegativity values of the complexes is little bit equal to each other. The order is Complex B > Complex A > Complex C. Thus the Complex B show the highest value of electronegativity.

Table 5.35. Electronegativity (χ) of the Complexes (A, B and C) By DFT/B3LYP level.

Electronegativity (χ) of the Complexes (A, B and C) By DFT/B3LYP level					
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G	Average
Complex A	3.630	3.767	3.767	3.941	3.777
Complex B	3.897	4.051	4.051	4.221	4.055
Complex C	3.447	3.599	3.599	3.785	3.607

5.2.5.4 Global Hardness (η) and Global Softness (S)

(Table 5.36) shows the calculated global hardness and global softness of the three complexes and the average of using several basis sets.

It is shown from the calculations that Complex B has in average the highest hardness and the lowest softness with 2.223 and 0.45 respectively. Meanwhile, Complex C has in average the highest softness and the lowest hardness with 0.585 and 1.718 respectively.

Table 5.36. Global Hardness (η) and Global softness(S) eV of the Complexes (A, B and C) By DFT/B3LYP level.

Global Hardness (η)					
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G	Average
Complex A	2.261	2.190	2.190	2.184	2.206
Complex B	2.272	2.208	2.208	2.202	2.223
Complex C	1.732	1.714	1.714	1.711	1.718
Global Softness (S)					
DFT/B3LYP	3-21G	6-31G	6-31G++dp	6-311G	Average
Complex A	0.442	0.457	0.457	0.458	0.453
Complex B	0.440	0.453	0.453	0.454	0.450
Complex C	0.577	0.583	0.583	0.585	0.582

5.3 COMPUTATIONAL INSIGHT TO THE REACTION PATH WAY

The procedure for the synthesis of cisplatin is starting from Potassium tetrachloroplatinate which converted to Potassium tetraiodoplatinate analogue by the addition of saturated solution of Potassium iodide, and then the Ammonia is added (Alderden, Hall, & Hambley, 2006).

In this study the Ammonia will be replaced with Adenine, and the predicted reaction pathway of synthesizing the novel cisplatin derivative (Complex A) will be studied (Figure 5.9).

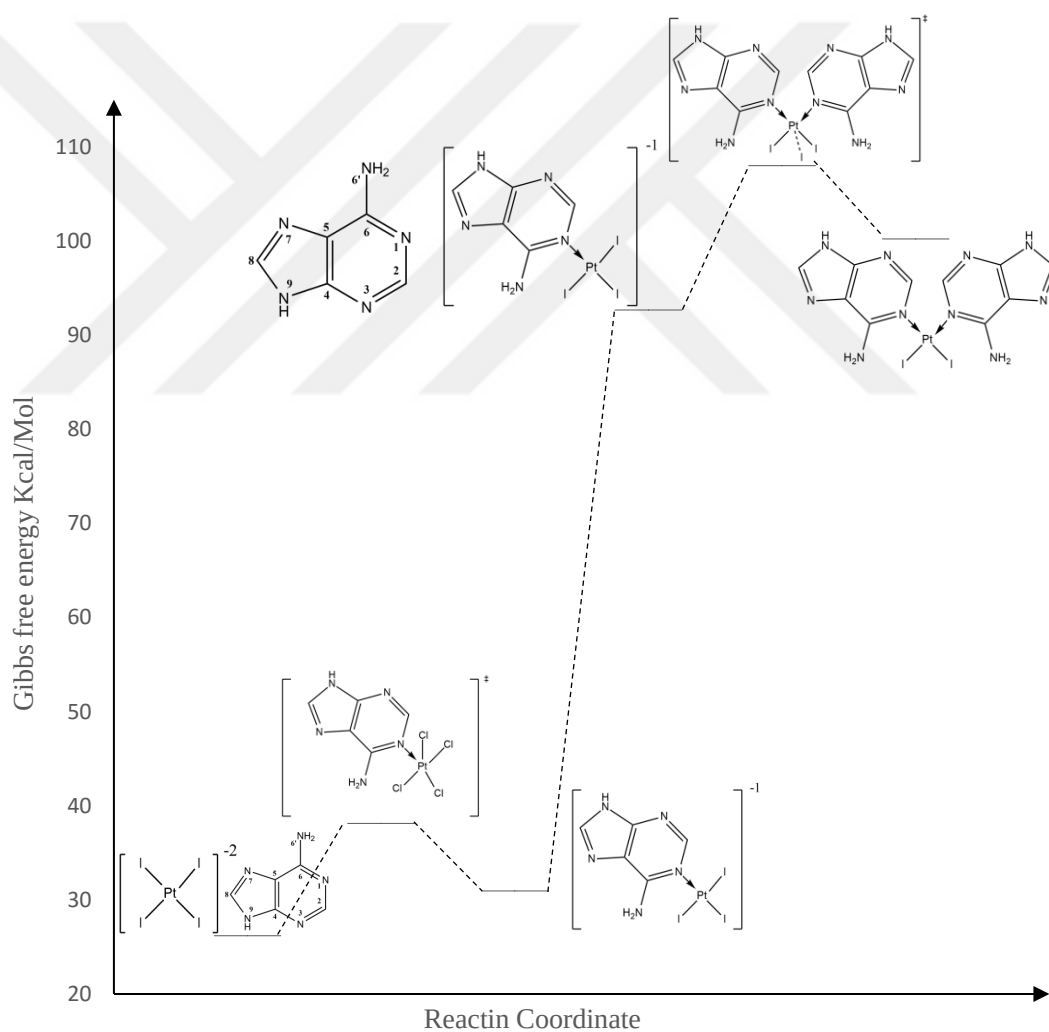


Figure 5.9. Predicted Reaction pathway of synthesizing complex A.

The computational prediction of the reaction pathway done using DFT/B3LYP method. And 3-21G basis set used for (H, C, and N) atoms, 6-311G++dp basis set taken from Basis Set Exchange website (Feller, 2007) is used for Iodine atom (Appendix D), and for platinum atom two basis sets have been used, Stuttgart/Dresden (SDD) basis set used for outer shell electrons, and Los Alamos National Laboratory 2 (LANL2) basis set (effective core potentials) used for the core electrons.

In this prediction the DNA Nucleobase (Adenine) attack the metal core (Pt II) using the nitrogen atom in position (N1) as a nucleophile and the Iodine leaving group will be replaced.

The reaction mechanism predicted to follow SN2 mechanism (Back Side Attack) (Figure 5.10).

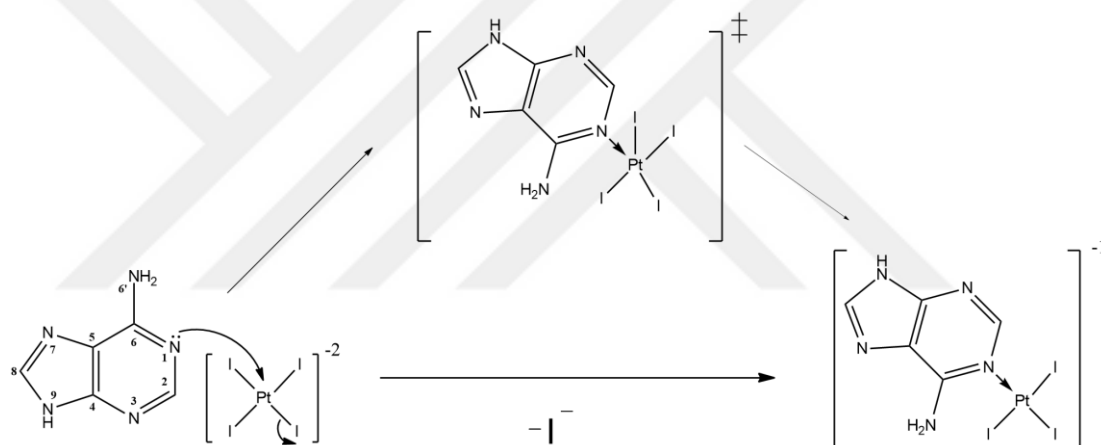


Figure 5.10. Reaction mechanism of synthesizing complex A.

The reaction predicted to be with two steps, the first step (Figure 5.11) predicted to be non-spontaneous process since the $\Delta G_1 = 4.79$ Kcal/Mol is positive Value.

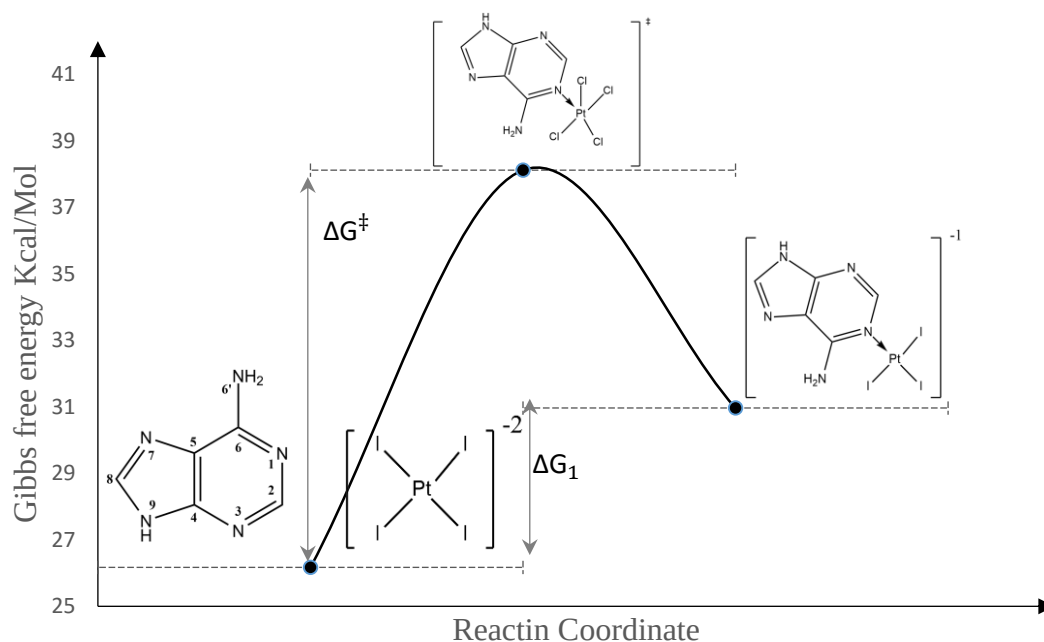


Figure 5.11. Predicted First step of synthesizing complex A.

In the second step (Figure 5.12) the reaction predicted to be non-spontaneous process too with $\Delta G_2 = 11.94$ Kcal/Mol which is positive Value.

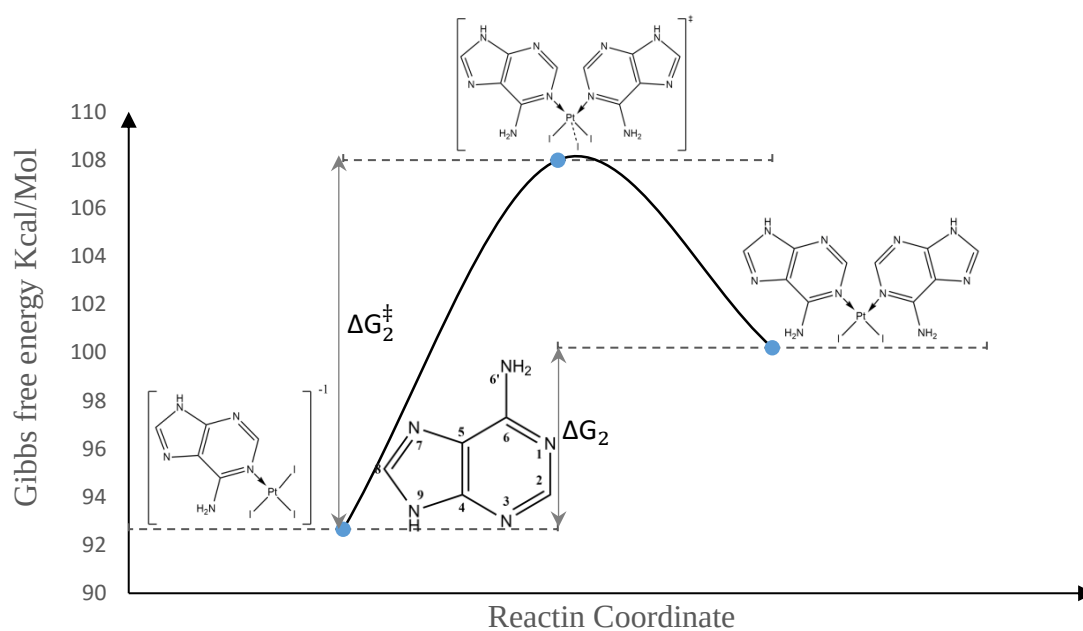


Figure 5. 12. Predicted Second step of synthesizing complex A.

6. CONCLUSION

Quantum mechanical method employing DFT/B3LYP and several basis sets were good to investigate the properties of the pyrimidine and its derivatives with the DNA (Adenine, Guanine, Cytosine and Thymine). The results of bond lengths, bond angles, total energy, dipole moment and HOMO-LUNO were very good comparing to the experimental data.

In addition, the novel complexes of platinum (II) with Adenine and Cytosine (complex A, complex B and complex C) showed square planar geometry and good results comparing with cisplatin. Moreover the calculations of frequency showed positive result for all complexes (no imaginary frequency) so the all complexes are expected to be stable.

After all, the reaction of synthesizing the (complex A) predicted to be non-spontaneous process with positive Values of ΔG Gibbs free energy.

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APPENDICES

7. APPENDICES

Appendix A. Calculated bond lengths of the DNA nucleobases by Hartree-fock method using several basis sets:

Table A.1. Adenine bond lengths By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.3390	1.3366	1.3390	1.3291	1.3307
C2-N3	1.3310	1.3244	1.3254	1.3136	1.3154
N3-C4	1.3440	1.3321	1.3368	1.3288	1.3305
C4-C5	1.3830	1.3814	1.3824	1.3765	1.3780
C5-C6	1.4060	1.3953	1.3986	1.4015	1.4025
C6-N1	1.3510	1.3336	1.3389	1.3274	1.3293
C5-N7	1.3880	1.3949	1.3914	1.3826	1.3863
N7-C8	1.3110	1.2928	1.2954	1.2818	1.2837
C8-N9	1.3730	1.3892	1.3816	1.3707	1.3723
N9-C6	1.3740	1.3673	1.3655	1.3621	1.3650
C6-N6	1.3350	1.3392	1.3422	1.3412	1.3444

Table A.2. Guanine bond lengths By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.373	1.3642	1.3671	1.3597	1.3592
C2-N3	1.323	1.2996	1.3041	1.2924	1.2947
N3-C4	1.35	1.3547	1.3596	1.354	1.3558
C4-C5	1.379	1.371	1.3741	1.3697	1.3715
C5-C6	1.419	1.4247	1.4254	1.4345	1.4353
C6-N1	1.391	1.4265	1.4169	1.4152	1.4155
C5-N7	1.388	1.3918	1.387	1.3785	1.3827
N7-C8	1.305	1.2903	1.2928	1.2788	1.2806
C8-N9	1.374	1.3956	1.3875	1.3758	1.3774
N9-C4	1.375	1.3553	1.3548	1.3523	1.3554
C2-N2	1.341	1.3456	1.3482	1.3485	1.3512
C6-O6	1.237	1.2116	1.2215	1.1959	1.1959

Table A.3. Cytosine bond lengths By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.397	1.4149	1.4042	1.4008	1.4007
C2-N3	1.353	1.3684	1.3677	1.361	1.3625
N3-C4	1.335	1.2974	1.3088	1.2983	1.3008
C4-C5	1.425	1.4432	1.4422	1.4452	1.4458
C5-C6	1.339	1.3376	1.3436	1.3407	1.3427
C6-N1	1.367	1.3544	1.357	1.3482	1.3486
C2-O2	1.24	1.2113	1.2234	1.1993	1.1996
C4-N4	1.335	1.3439	1.3446	1.3435	1.3462

Table A.4. Thymine bond lengths By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
N1-C2	1.376	1.3736	1.3685	1.3667	1.3681
C2-N3	1.373	1.3734	1.3707	1.3697	1.3698
N3-C4	1.382	1.3899	1.3881	1.3867	1.3877
C4-C5	1.445	1.465	1.4645	1.4715	1.4719
C5-C6	1.339	1.3266	1.3355	1.3315	1.3337
C6-N1	1.378	1.3805	1.382	1.3781	1.3785
C2-O2	1.22	1.2119	1.223	1.1969	1.1972
C4-O4	1.228	1.2141	1.2229	1.1968	1.1968
C5-Me5	1.496	1.51	1.506	1.5026	1.503

Appendix B. Calculated bond angles of Adenine by Hartree-fock method using several basis sets:

Table B.1. Adenine bond angles By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
C6-N1-C2	118.6	119.87733	119.83092	118.74065	118.51452
N1-C2-N3	129.3	126.43843	126.70841	128.53914	128.78116
C2-N3-C4	110.6	113.45007	113.11857	111.71629	111.53111
N3-C4-C5	126.8	125.07466	125.34568	126.44123	126.52929
C4-C5-C6	117	117.21681	117.19066	116.11718	116.06973
C5-C6-N1	117.7	117.94271	117.80576	118.4455	118.57418
C4-C5-N7	110.7	110.09395	110.15025	110.91406	110.88709
C5-N7-C8	103.9	105.4043	105.21825	104.25037	104.20903
N7-C8-N9	113.8	112.15852	112.28019	113.49366	113.55529
C8-N9-C4	105.8	106.83627	106.98882	106.5171	106.4893
N9-C4-C5	105.8	105.50696	105.36248	104.8248	104.85929
N3-C4-N9	127.4	129.41839	129.29184	128.73397	128.61142
C6-C5-N7	132.3	132.68924	123.17584	132.96877	133.04318
N1-C6-N6	118.6	119.42549	119.01839	119.04437	118.92451
C5-C6-N6	123.7	122.6318	123.17584	122.51012	122.50131

Table B.2. Guanine bond angles By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-Pvdz
N7-C8-N9	113.1	111.2938	111.5563	112.7776	112.8302
C8-N7-C5	104.3	105.9342	105.7139	104.7995	104.7730
N7-C5-C6	130.4	130.5032	130.8178	130.9426	131.1265
N7-C5-C4	110.8	109.7413	109.8345	110.5478	110.5052
C6-C5-C4	118.8	119.7555	119.3477	118.5096	118.3683
C5-C6-O	128.6	131.3704	130.6619	131.1692	131.1380
C5-C6-N1	111.5	109.8766	110.5645	109.9142	110.0058
O-C6-N1	119.9	118.7531	118.7734	118.9167	118.8561
N1-C2-N3	123.9	122.6562	122.7747	123.6599	123.8453
N3-C2-N2	119.9	119.7858	119.6817	119.5936	119.4672
N1-C2-N2	116.2	117.5580	117.5436	116.7465	116.6875
C2-N3-C4	111.9	114.2980	114.0450	112.8021	112.5300
N3-C4-C5	128.6	127.3871	127.4173	128.9238	129.0987
C5-C4-N9	105.4	106.1524	105.9409	105.3438	105.3609
N3-C4-N9	126	126.4605	126.6417	125.7324	125.5404
C8-N9-C4	106.4	106.8783	106.9544	106.5312	106.5306
C6-N1-C2	125.1	126.0266	125.8507	109.9142	126.1519

Table B.3. Cytosine bond angles By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
C6-N1-C2	120.3	122.9296	123.0474	123.0774	123.0280
N1-C6-C5	121	120.8037	120.3648	120.3971	120.4311
C6-C5-C4	117.4	116.0858	116.3256	115.6237	115.5326
C5-C4-N4	120.2	119.1717	119.6503	118.6046	118.5453
C5-C4-N3	121.9	122.7474	122.7328	123.7584	123.9503
N4-C4-N3	118	118.0810	117.6169	117.6370	117.5044
C4-N3-C2	119.9	122.2487	121.4191	120.4431	120.1221
N1-C2-N3	119.2	115.1849	116.1104	116.7003	116.9359
N1-C2-O	118.9	118.9114	118.6920	118.2333	118.1943
N3-C2-O	121.9	125.9037	125.1976	125.0664	124.8698

Table B.4. Thymine bond angles By HF.

HF	Experimental	3-21G	6-31G	6-31G++dp	aug-cc-pVDZ
C6-N1-C2	121.3	123.1292	123.2481	123.3541	123.2737
N1-C6-C5	123.7	123.1079	122.8294	122.9953	123.0441
C6-C5-Me	122.9	124.2492	123.7720	124.4034	124.3712
C4-C5-C6	118	118.0861	117.5591	117.4655	117.3423
Me-C5-C4	119	117.6647	118.6689	118.1311	118.2865
C5-C4-O4	124.9	124.9719	124.7418	124.5896	124.5404
C5-C4-N3	115.2	114.5477	115.3709	115.1135	115.2949
O4-C4-N3	119.9	120.4803	119.8874	120.2969	120.1648
C4-N3-C2	127.2	128.0461	127.3353	127.4565	127.2815
N1-C2-N3	114.6	113.0830	113.6572	113.6152	113.7636
N1-C2-O2	123.1	123.2566	123.0512	123.1187	123.0180
N3-C2-O2	122.3	123.6604	123.2916	123.2661	123.2184

Appendix C. Example of input/output files by Gaussian program.

Appendix C.1. Input file of the Complex A.

```
%nprocshared=4
%lindaworkers=:1
%mem=600MB
%chk
#p opt freq=noraman rb3lyp/genecp scrf=check geom=connectivity
int=ultrafine output=pickett pseudo=read
```

CisPlatin

```
0 1
Pt      0.00002383 -1.27221257 -0.00008831
Cl      1.68212443 -2.93368928 -0.33117927
Cl      -1.68250922 -2.93315077  0.33123459
N       -1.44383090  0.19140425  0.28632639
C       -2.47112331  0.36914159 -0.61020874
C       -1.36724389  0.97769168  1.41182392
C       -3.38329141  1.40679576 -0.32133323
N       -2.57607785 -0.40093156 -1.70373601
H       -0.54593650  0.75729152  2.07687544
N       -2.19714626  1.96466482  1.74670758
N       -4.51060057  1.84658520 -1.01510997
C       -3.19377145  2.14886849  0.84868694
H       -2.02264885 -1.24773477 -1.77067221
H       -3.36683701 -0.27025223 -2.31705298
C       -4.99072118  2.83672407 -0.27407901
N       -4.22788688  3.06137143  0.86959939
H       -5.86825977  3.41709593 -0.50463062
H       -4.39215451  3.74562426  1.59122632
N       1.44409310  0.19128132 -0.28640879
C       2.47178762  0.36858905  0.60976330
C       1.36685293  0.97835455 -1.41132707
C       3.38352803  1.40673510  0.32123975
N       2.57756556 -0.40229013  1.70262534
H       0.54528453  0.75827554 -2.07616150
N       2.19632666  1.96580763 -1.74585391
N       4.51100469  1.84632183  1.01487179
C       3.19328477  2.14964487 -0.84811863
H       2.02460500 -1.24943899  1.76915567
H       3.36851932 -0.27167467  2.31570826
C       4.99053464  2.83715252  0.27438013
N       4.22714959  3.06244094 -0.86880524
H       5.86800571  3.41760098  0.50499533
H       4.39090423  3.74729736 -1.58997580
```

```
1 2 1.0 3 1.0 4 1.0 19 1.0
2
3
4 5 2.0 6 1.0
5 7 1.0 8 1.0
6 9 1.0 10 2.0
7 11 1.0 12 2.0
8 13 1.0 14 1.0
9
10 12 1.0
```

Appendix C.1. Input file of the Complex A (Continued).

```
11 15 2.0
12 16 1.0
13
14
15 17 1.0 16 1.0
16 18 1.0
17
18
19 20 2.0 21 1.0
20 22 1.0 23 1.0
21 24 1.0 25 2.0
22 26 1.0 27 2.0
23 28 1.0 29 1.0
24
25 27 1.0
26 30 2.0
27 31 1.0
28
29
30 32 1.0 31 1.0
31 33 1.0
32
33
```

N CL C H 0

6-311G

1 0

SDD

1 0

LANL2

Appendix C.2. Output file of the Complex A. The bond lengths, bond angles and dihedrals after completing the optimization.

Optimization completed.
 -- Stationary point found.

 ! Optimized Parameters !
 ! (Angstroms and Degrees) !

!	Name	Definition	Value	Derivative	Info.	!

!	R1	R(1,2)	2.39	-DE/DX =	0	!
!	R2	R(1,3)	2.39	-DE/DX =	0	!
!	R3	R(1,4)	2.0777	-DE/DX =	0	!
!	R4	R(1,19)	2.0777	-DE/DX =	0	!
!	R5	R(4,5)	1.3753	-DE/DX =	0	!
!	R6	R(4,6)	1.3744	-DE/DX =	0	!
!	R7	R(5,7)	1.4093	-DE/DX =	0	!
!	R8	R(5,8)	1.3407	-DE/DX =	0	!
!	R9	R(6,9)	1.0759	-DE/DX =	0	!
!	R10	R(6,10)	1.3312	-DE/DX =	0	!
!	R11	R(7,11)	1.3957	-DE/DX =	0	!
!	R12	R(7,12)	1.394	-DE/DX =	0	!
!	R13	R(8,13)	1.0105	-DE/DX =	0	!
!	R14	R(8,14)	1.0064	-DE/DX =	0	!
!	R15	R(10,12)	1.3549	-DE/DX =	0	!
!	R16	R(11,15)	1.3254	-DE/DX =	0	!
!	R17	R(12,16)	1.3788	-DE/DX =	0	!
!	R18	R(15,16)	1.391	-DE/DX =	0	!
!	R19	R(15,17)	1.0739	-DE/DX =	0	!
!	R20	R(16,18)	1.0051	-DE/DX =	0	!
!	R21	R(19,20)	1.3753	-DE/DX =	0	!
!	R22	R(19,21)	1.3744	-DE/DX =	0	!
!	R23	R(20,22)	1.4093	-DE/DX =	0	!
!	R24	R(20,23)	1.3407	-DE/DX =	0	!
!	R25	R(21,24)	1.0759	-DE/DX =	0	!
!	R26	R(21,25)	1.3312	-DE/DX =	0	!
!	R27	R(22,26)	1.3957	-DE/DX =	0	!
!	R28	R(22,27)	1.394	-DE/DX =	0	!
!	R29	R(23,28)	1.0105	-DE/DX =	0	!
!	R30	R(23,29)	1.0064	-DE/DX =	0	!
!	R31	R(25,27)	1.3549	-DE/DX =	0	!
!	R32	R(26,30)	1.3254	-DE/DX =	0	!
!	R33	R(27,31)	1.3788	-DE/DX =	0	!
!	R34	R(30,31)	1.391	-DE/DX =	0	!

Appendix C.2. Output file of the Complex A. The bond lengths, bond angles and dihedrals after completing the optimization (Continued).

!	R35	R(30,32)	1.0739	-DE/DX =	0	!
!	R36	R(31,33)	1.0051	-DE/DX =	0	!
!	A1	A(2,1,3)	91.4915	-DE/DX =	0	!
!	A2	A(2,1,19)	89.1125	-DE/DX =	0	!
!	A3	A(3,1,4)	89.1121	-DE/DX =	0	!
!	A4	A(4,1,19)	90.2839	-DE/DX =	0	!
!	A5	A(1,4,5)	121.4423	-DE/DX =	0	!
!	A6	A(1,4,6)	118.4788	-DE/DX =	0	!
!	A7	A(5,4,6)	120.0734	-DE/DX =	0	!
!	A8	A(4,5,7)	116.3018	-DE/DX =	0	!
!	A9	A(4,5,8)	121.1322	-DE/DX =	0	!
!	A10	A(7,5,8)	122.5623	-DE/DX =	0	!
!	A11	A(4,6,9)	115.5317	-DE/DX =	0	!
!	A12	A(4,6,10)	126.4637	-DE/DX =	0	!
!	A13	A(9,6,10)	118.0047	-DE/DX =	0	!
!	A14	A(5,7,11)	130.5404	-DE/DX =	0	!
!	A15	A(5,7,12)	118.4622	-DE/DX =	0	!
!	A16	A(11,7,12)	110.9939	-DE/DX =	0	!
!	A17	A(5,8,13)	119.6808	-DE/DX =	0	!
!	A18	A(5,8,14)	118.8387	-DE/DX =	0	!
!	A19	A(13,8,14)	119.492	-DE/DX =	0	!
!	A20	A(6,10,12)	113.0933	-DE/DX =	0	!
!	A21	A(7,11,15)	104.4615	-DE/DX =	0	!
!	A22	A(7,12,10)	125.5836	-DE/DX =	0	!
!	A23	A(7,12,16)	105.2412	-DE/DX =	0	!
!	A24	A(10,12,16)	129.1725	-DE/DX =	0	!
!	A25	A(11,15,16)	112.3304	-DE/DX =	0	!
!	A26	A(11,15,17)	125.1589	-DE/DX =	0	!
!	A27	A(16,15,17)	122.5106	-DE/DX =	0	!
!	A28	A(12,16,15)	106.9729	-DE/DX =	0	!
!	A29	A(12,16,18)	125.4126	-DE/DX =	0	!
!	A30	A(15,16,18)	127.6102	-DE/DX =	0	!
!	A31	A(1,19,20)	121.4425	-DE/DX =	0	!
!	A32	A(1,19,21)	118.4787	-DE/DX =	0	!
!	A33	A(20,19,21)	120.0734	-DE/DX =	0	!
!	A34	A(19,20,22)	116.3018	-DE/DX =	0	!
!	A35	A(19,20,23)	121.1324	-DE/DX =	0	!
!	A36	A(22,20,23)	122.5621	-DE/DX =	0	!
!	A37	A(19,21,24)	115.5317	-DE/DX =	0	!
!	A38	A(19,21,25)	126.4638	-DE/DX =	0	!
!	A39	A(24,21,25)	118.0046	-DE/DX =	0	!
!	A40	A(20,22,26)	130.5403	-DE/DX =	0	!

Appendix C.2. Output file of the Complex A. The bond lengths, bond angles and dihedrals after completing the optimization (Continued).

!	A41	A(20,22,27)	118.4623	-DE/DX =	0	!
!	A42	A(26,22,27)	110.994	-DE/DX =	0	!
!	A43	A(20,23,28)	119.6811	-DE/DX =	0	!
!	A44	A(20,23,29)	118.8386	-DE/DX =	0	!
!	A45	A(28,23,29)	119.4919	-DE/DX =	0	!
!	A46	A(21,25,27)	113.0933	-DE/DX =	0	!
!	A47	A(22,26,30)	104.4615	-DE/DX =	0	!
!	A48	A(22,27,25)	125.5836	-DE/DX =	0	!
!	A49	A(22,27,31)	105.2413	-DE/DX =	0	!
!	A50	A(25,27,31)	129.1725	-DE/DX =	0	!
!	A51	A(26,30,31)	112.3304	-DE/DX =	0	!
!	A52	A(26,30,32)	125.1589	-DE/DX =	0	!
!	A53	A(31,30,32)	122.5106	-DE/DX =	0	!
!	A54	A(27,31,30)	106.9728	-DE/DX =	0	!
!	A55	A(27,31,33)	125.4126	-DE/DX =	0	!
!	A56	A(30,31,33)	127.6102	-DE/DX =	0	!
!	D1	D(3,1,4,5)	-66.6661	-DE/DX =	0	!
!	D2	D(3,1,4,6)	112.4837	-DE/DX =	0	!
!	D3	D(19,1,4,5)	113.3306	-DE/DX =	0	!
!	D4	D(19,1,4,6)	-67.5196	-DE/DX =	0	!
!	D5	D(2,1,19,20)	-66.658	-DE/DX =	0	!
!	D6	D(2,1,19,21)	112.4938	-DE/DX =	0	!
!	D7	D(4,1,19,20)	113.3391	-DE/DX =	0	!
!	D8	D(4,1,19,21)	-67.5092	-DE/DX =	0	!
!	D9	D(1,4,5,7)	-179.0976	-DE/DX =	0	!
!	D10	D(1,4,5,8)	0.2204	-DE/DX =	0	!
!	D11	D(6,4,5,7)	1.766	-DE/DX =	0	!
!	D12	D(6,4,5,8)	-178.916	-DE/DX =	0	!
!	D13	D(1,4,6,9)	-0.6572	-DE/DX =	0	!
!	D14	D(1,4,6,10)	179.3133	-DE/DX =	0	!
!	D15	D(5,4,6,9)	178.5046	-DE/DX =	0	!
!	D16	D(5,4,6,10)	-1.5249	-DE/DX =	0	!
!	D17	D(4,5,7,11)	179.628	-DE/DX =	0	!
!	D18	D(4,5,7,12)	-1.1148	-DE/DX =	0	!
!	D19	D(8,5,7,11)	0.3207	-DE/DX =	0	!
!	D20	D(8,5,7,12)	179.5779	-DE/DX =	0	!
!	D21	D(4,5,8,13)	13.4959	-DE/DX =	0	!
!	D22	D(4,5,8,14)	177.3807	-DE/DX =	0	!
!	D23	D(7,5,8,13)	-167.2295	-DE/DX =	0	!
!	D24	D(7,5,8,14)	-3.3447	-DE/DX =	0	!
!	D25	D(4,6,10,12)	0.4317	-DE/DX =	0	!
!	D26	D(9,6,10,12)	-179.5985	-DE/DX =	0	!

Appendix C.2. Output file of the Complex A. The bond lengths, bond angles and dihedrals after completing the optimization (Continued).

!	D27	D(5,7,11,15)	179.2724	-DE/DX =	0	!
!	D28	D(12,7,11,15)	-0.0281	-DE/DX =	0	!
!	D29	D(5,7,12,10)	0.0907	-DE/DX =	0	!
!	D30	D(5,7,12,16)	-179.3611	-DE/DX =	0	!
!	D31	D(11,7,12,10)	179.4861	-DE/DX =	0	!
!	D32	D(11,7,12,16)	0.0343	-DE/DX =	0	!
!	D33	D(6,10,12,7)	0.2834	-DE/DX =	0	!
!	D34	D(6,10,12,16)	179.6012	-DE/DX =	0	!
!	D35	D(7,11,15,16)	0.0108	-DE/DX =	0	!
!	D36	D(7,11,15,17)	-179.9217	-DE/DX =	0	!
!	D37	D(7,12,16,15)	-0.0263	-DE/DX =	0	!
!	D38	D(7,12,16,18)	179.2594	-DE/DX =	0	!
!	D39	D(10,12,16,15)	-179.4512	-DE/DX =	0	!
!	D40	D(10,12,16,18)	-0.1655	-DE/DX =	0	!
!	D41	D(11,15,16,12)	0.0101	-DE/DX =	0	!
!	D42	D(11,15,16,18)	-179.255	-DE/DX =	0	!
!	D43	D(17,15,16,12)	179.9446	-DE/DX =	0	!
!	D44	D(17,15,16,18)	0.6795	-DE/DX =	0	!
!	D45	D(1,19,20,22)	-179.0948	-DE/DX =	0	!
!	D46	D(1,19,20,23)	0.2232	-DE/DX =	0	!
!	D47	D(21,19,20,22)	1.7668	-DE/DX =	0	!
!	D48	D(21,19,20,23)	-178.9152	-DE/DX =	0	!
!	D49	D(1,19,21,24)	-0.6595	-DE/DX =	0	!
!	D50	D(1,19,21,25)	179.3106	-DE/DX =	0	!
!	D51	D(20,19,21,24)	178.5042	-DE/DX =	0	!
!	D52	D(20,19,21,25)	-1.5257	-DE/DX =	0	!
!	D53	D(19,20,22,26)	179.6268	-DE/DX =	0	!
!	D54	D(19,20,22,27)	-1.1151	-DE/DX =	0	!
!	D55	D(23,20,22,26)	0.3195	-DE/DX =	0	!
!	D56	D(23,20,22,27)	179.5775	-DE/DX =	0	!
!	D57	D(19,20,23,28)	13.4968	-DE/DX =	0	!
!	D58	D(19,20,23,29)	177.3818	-DE/DX =	0	!
!	D59	D(22,20,23,28)	-167.2286	-DE/DX =	0	!
!	D60	D(22,20,23,29)	-3.3436	-DE/DX =	0	!
!	D61	D(19,21,25,27)	0.4319	-DE/DX =	0	!
!	D62	D(24,21,25,27)	-179.5987	-DE/DX =	0	!
!	D63	D(20,22,26,30)	179.2716	-DE/DX =	0	!
!	D64	D(27,22,26,30)	-0.0298	-DE/DX =	0	!
!	D65	D(20,22,27,25)	0.0904	-DE/DX =	0	!
!	D66	D(20,22,27,31)	-179.3606	-DE/DX =	0	!
!	D67	D(26,22,27,25)	179.4864	-DE/DX =	0	!
!	D68	D(26,22,27,31)	0.0355	-DE/DX =	0	!

Appendix C.2. Output file of the Complex A. The bond lengths, bond angles and dihedrals after completing the optimization (Continued).

!	D69	D(21,25,27,22)	0.2839	-DE/DX =	0	!
!	D70	D(21,25,27,31)	179.6006	-DE/DX =	0	!
!	D71	D(22,26,30,31)	0.0123	-DE/DX =	0	!
!	D72	D(22,26,30,32)	-179.9212	-DE/DX =	0	!
!	D73	D(22,27,31,30)	-0.0265	-DE/DX =	0	!
!	D74	D(22,27,31,33)	179.2591	-DE/DX =	0	!
!	D75	D(25,27,31,30)	-179.4505	-DE/DX =	0	!
!	D76	D(25,27,31,33)	-0.1649	-DE/DX =	0	!
!	D77	D(26,30,31,27)	0.0092	-DE/DX =	0	!
!	D78	D(26,30,31,33)	-179.2558	-DE/DX =	0	!
!	D79	D(32,30,31,27)	179.9448	-DE/DX =	0	!
!	D80	D(32,30,31,33)	0.6797	-DE/DX =	0	!

Appendix D. Basis set used for Iodine Atom.

6-311G++dp basis set taken from Basis Set Exchange website (Feller, 2007)

```
I 0
S 5 1.00
444750.0000000 0.0008900
66127.0000000 0.0069400
14815.0000000 0.0360900
4144.9000000 0.1356800
1361.2000000 0.3387800
S 2 1.00
508.4400000 0.4365900
209.5900000 0.1837500
S 1 1.00
81.9590000 1.0000000
S 1 1.00
36.8050000 1.0000000
S 1 1.00
13.4950000 1.0000000
S 1 1.00
6.8859000 1.0000000
S 1 1.00
2.5520000 1.0000000
S 1 1.00
1.2088000 1.0000000
S 1 1.00
0.2734000 1.0000000
S 1 1.00
0.1009000 1.0000000
P 4 1.00
2953.6000000 0.0122100
712.6100000 0.0858700
236.7100000 0.2949300
92.6310000 0.4784900
P 1 1.00
39.7320000 1.0000000
P 1 1.00
17.2730000 1.0000000
P 1 1.00
7.9570000 1.0000000
P 1 1.00
3.1529000 1.0000000
P 1 1.00
1.3328000 1.0000000
P 1 1.00
0.4947000 1.0000000
P 1 1.00
0.2160000 1.0000000
P 1 1.00
0.0829300 1.0000000
D 3 1.00
261.9500000 0.0314400
76.7340000 0.1902800
27.5510000 0.4724700
```

6-311G++dp basis set taken from Basis Set Exchange website (Feller, 2007)
(Continued).

```
D 1 1.00
    10.6060000    1.0000000
D 1 1.00
    3.4217000    1.0000000
D 1 1.00
    1.1370000    1.0000000
D 1 1.00
    0.3020000    1.0000000
****
I 0
D 1 1.00
    0.3020000    1.0000000
```

Appendix E: Mathematical calculation of the mean absolute percentage error (MAPE %):

$$\text{MAPE \%} = \frac{100}{n} \sum_{t=1}^n \left| \frac{A_t - F_t}{A_t} \right| \quad (\text{E.1})$$

A_t : The experimental value.

F_t : The Calculated value.

n : The number of fitted points.

Appendix F: Mathematical calculation of the Percent error (%error):

$$\% \text{error} = \left| \frac{\text{Calculated Value} - \text{Experimental value}}{\text{Experimental value}} \right| \times 100 \quad (\text{F.2})$$

Appendix G: Some frequencies values calculated by DFT/B3LYP method and 6-311G basis set:

Table G.1. Some frequencies values for the **Complex A** calculated by DFT/B3LYP method and 6-311G basis set.

	Frequencies	Red. masses	Frc consts	IR Inten
1	21.9947	7.674	0.0022	1.0316
2	25.0353	6.3455	0.0023	0.4906
3	35.4707	6.5347	0.0048	0.2989
4	46.1903	9.2592	0.0116	0.5558
5	56.6804	19.3952	0.0367	0.005
6	94.5396	14.9113	0.0785	2.8007
7	113.2077	6.5627	0.0496	0.4571
8	134.8155	9.7985	0.1049	0.3388
9	144.0242	22.9423	0.2804	0.4712
10	160.5835	8.4527	0.1284	0.3843
11	175.3441	6.6088	0.1197	8.5939
12	184.8825	5.5203	0.1112	6.6656
13	191.7372	8.6302	0.1869	5.0007
14	202.7154	9.8415	0.2383	0.075
15	203.2525	10.1079	0.246	0.3188
16	258.6743	4.3888	0.173	6.7089
17	259.2932	4.3345	0.1717	1.8869
18	301.402	3.6624	0.196	39.756
19	302.7358	3.6888	0.1992	6.0958
20	326.4986	26.741	1.6795	29.326
21	334.6915	29.2214	1.9286	47.1954
22	353.5925	9.8028	0.7221	0.3053
23	368.9899	9.3363	0.7489	0.0381
24	533.6837	2.5751	0.4321	6.2007
25	536.4019	3.8446	0.6518	3.8648
26	543.0332	1.9896	0.3457	12.2303
27	551.8808	1.4552	0.2611	0.9804
28	558.0847	3.0464	0.559	4.7426
29	560.8725	2.612	0.4841	1.6881
30	574.7369	3.4702	0.6754	18.047

Table G.2. Some frequencies values for the **Complex B** calculated by DFT/B3LYP method and 6-311G basis set.

	Frequencies	Red. Masses	Frc consts	IR Inten
1	14.5701	6.4016	0.0008	0.6513
2	22.8465	8.0396	0.0025	0.0612
3	30.8018	6.5065	0.0036	0.039
4	51.1525	8.7242	0.0134	4.4667
5	51.7649	15.9141	0.0251	0.0934
6	84.9651	15.1275	0.0643	5.2155
7	103.7512	5.4122	0.0343	5.5925
8	120.8316	7.2417	0.0623	1.5347
9	126.1325	8.7665	0.0822	0.6041
10	143.7561	26.389	0.3213	0.2576
11	162.0235	14.4879	0.2241	3.6458
12	209.6442	6.5013	0.1684	1.9242
13	211.4388	5.7235	0.1508	2.6127
14	217.1004	5.8257	0.1618	9.4536
15	224.1109	7.5241	0.2227	1.2036
16	242.3017	8.9219	0.3086	1.5812
17	246.526	7.7044	0.2759	0.2719
18	330.1903	16.7142	1.0737	42.8782
19	337.9179	8.0115	0.539	26.9124
20	339.8359	6.4209	0.4369	7.5673
21	341.9125	7.299	0.5027	1.7369
22	346.9061	4.055	0.2875	11.4304
23	360.5929	6.0164	0.4609	0.0603
24	526.3545	4.3443	0.7091	0.1076
25	526.8388	5.0188	0.8207	1.0535
26	534.8547	2.1422	0.3611	22.9237
27	538.8628	3.603	0.6164	4.9836
28	556.8203	1.6174	0.2955	51.8556
29	561.535	1.2823	0.2382	1.12
30	567.1878	3.3666	0.6381	7.8453

Table G.3. Some frequencies values for the **Complex C** calculated by DFT/B3LYP method and 6-311G basis set.

	Frequencies	Red. masses	Frc consts	IR Inten
1	45.752	5.7608	0.0071	8.5041
2	52.02	6.597	0.0105	5.527
3	62.3463	7.2036	0.0165	4.4386
4	67.1578	17.8779	0.0475	0.4879
5	72.3139	9.3065	0.0287	0.4318
6	103.7511	9.442	0.0599	10.031
7	116.1653	7.2914	0.058	1.0736
8	134.4082	9.6216	0.1024	1.4482
9	140.3071	24.8483	0.2882	0.006
10	175.2761	7.719	0.1397	0.6042
11	180.55	4.3121	0.0828	5.3011
12	190.5674	5.9251	0.1268	5.8532
13	200.9262	7.1392	0.1698	3.4241
14	202.1499	15.1144	0.3639	1.4186
15	214.9505	9.2086	0.2507	11.7574
16	294.5261	6.4761	0.331	4.0261
17	313.8493	6.3431	0.3681	2.7662
18	324.3323	38.3783	2.3786	40.678
19	334.6926	26.8787	1.774	44.5597
20	417.1186	4.032	0.4133	5.2957
21	425.3496	4.1056	0.4376	8.3671
22	468.2764	2.7129	0.3505	1.6414
23	472.1012	2.4948	0.3276	0.1595
24	533.0906	1.271	0.2128	4.0835
25	538.6434	2.0268	0.3465	41.4173
26	542.6052	2.1099	0.366	21.0228
27	547.6422	4.2748	0.7554	30.9117
28	559.4194	6.0338	1.1125	15.0266
29	566.9423	5.7423	1.0875	5.3277
30	615.1521	7.8478	1.7497	6.0043

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