Journal of Medicinal and Nanomaterials Chemistry 1 (2020) 67-81

Journal of Medicinal and Nanomaterials Chemistry

Journal homepage: https://jmnc.samipubco.com/

Orginal Research Aricle

Computational approach of palladium (II) complex ions with binuclear diamine ligands thermo-physical, chemical, and biological properties: a dft study

Mohammad Jahidul Islam[a], Sunanda Paul[b], Ajoy Kumer[c,*], Md. Nuruzzaman Sarker[a]

[a] *Department of Physics, European University of Bangladesh, Dhaka-1216, Bangladesh*

[b] *Department of Biochemistry and Molecular Biology, University of Chittagong, Chittagong,Hathazari-4334, Bangladesh*

[c] *Department of Chemistry, European University of Bangladesh, Dhaka-1216, Bangladesh*

ARTICLE INFORMATION

Received: 30 August 2019
Received in revised: 17 September 2019
Accepted: 24 September 2019
Available online: 23 November 2019

DOI: 10.48309/JMNC.2020.1.7

KEYWORDS

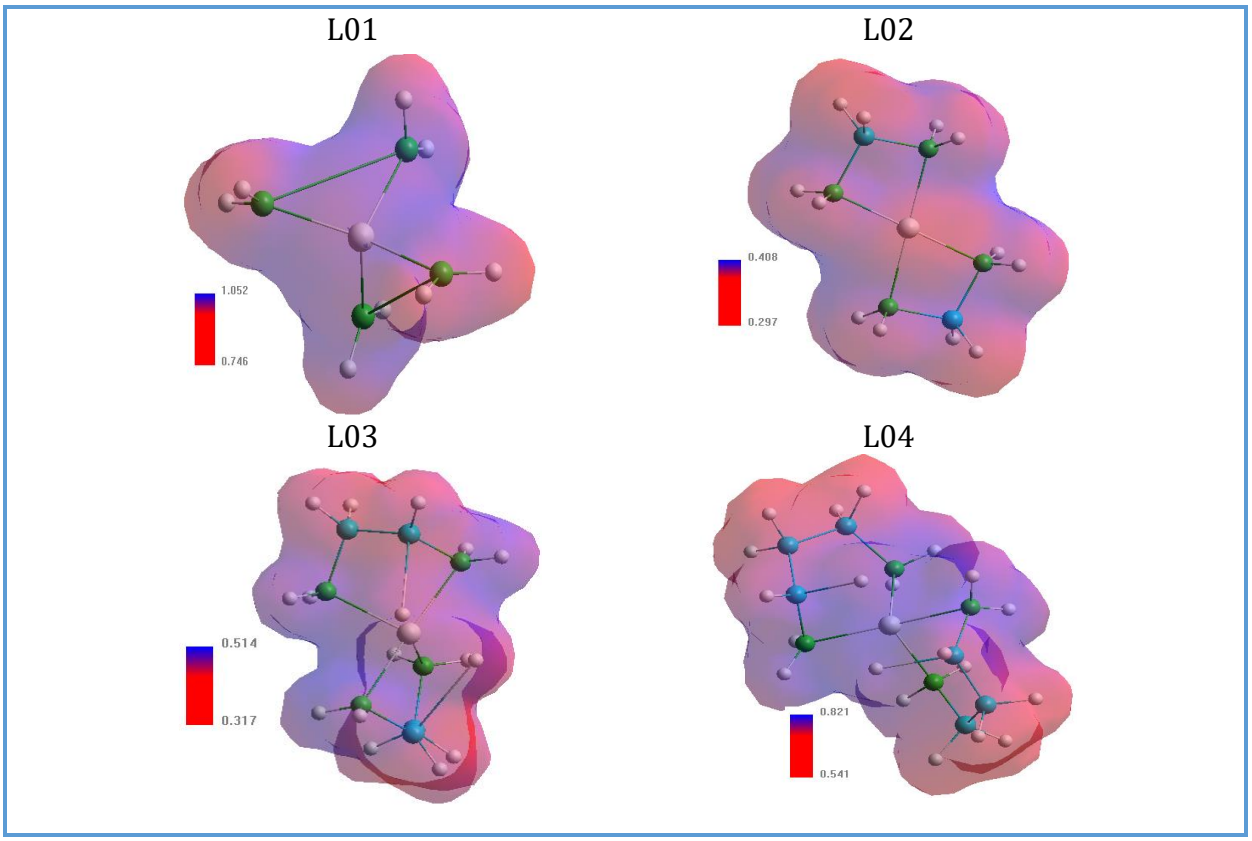
Palladium (II)
DFT
QSAR
HOMO
LUMO
Vibrational spectroscopy
Electronic spectroscopy

ABSTRACT

In computational chemistry through various basis sets, it is possible to design new molecules and discuss their use through their physical, chemical, biochemical studies. Chemical activity, biological activity, physical chemical activities can be diagnosed using density functional theory (DFT) for some palladium (II) complex ions. In this research study, the optimized dihydrazine palladium (II) complex ion (L01), di(1, 2- diaminemethane) palladium (II) complex ion (L02), di(1, 2- diamineethane) palladium (II) complex ion (L03), and di (1, 2- diamine propane) palladium (II) complex ion (L04) were simulated. Finally a comparative study of the palladium (II) complex ions were designed to show what ions are biologically more active using their QSAR data and orbital diagrams for HOMO and LUMO of the study of electronic properties. The HOMO-LUMO gap was also evaluated for chemical reactivity. The PIC50 value was calculated using the QSAR data where the value of L01, L02, and L03 L04 where -15.757, 13.128, -6.111 and -5.955, respectively. If PIC50 is below -6, then the compound is said to be biologically active. It was found that, the L04 is highly biological active and L03 is almost similar to L04. Also, by enhancing the methyl group in palladium chain, the biological activity increased.

Corresponding author, email: kumarajoy.cu@gmail.com (A. Kumer).
Tel.: +8801770568699.

Graphical Abstract



Introduction

Palladium (II) complexes are currently being widely used worldwide for cancer treatment, so the palladium (II) complexes have been brought to the center of research as target molecule to design anti-cancer drugs. Palladium is known as the versatile catalyst for coupling reaction in organic chemistry and useful metal in the chemical industry [1]. palladium (II) complex ions have low cytotoxicity [2] and anticancer properties against different cancer cell [3]. To estimate the biological activity of palladium (II) complex ions, some computing method from computational chemistry overviews was performed to calculate different properties. The thermo-physical, chemical reactivity and biological interaction are considered the most expected parameters in any area of chemical industry, pharmaceutical industry and academia [4, 5].

Due to the widespread applications of the density functional theory (DFT) in the field of chemistry, material science, and drug design in the last 30 years, it has been applied to organometallics and co-ordinate chemistry to develop the theoretical concept for the palladium ligand based complexes [6–12]. It is probably impossible to enumerate all the achievements made in cooperation between these two fields. Due to gain the Nobel Prize awarded in 2010 to Heck, Negishi, and Suzuki for palladium-catalyzed cross-coupling reactions for the widely used class of transformation of organic synthesis, the experimental work was being a lot in the last ten years [13, 14]. However, there have been

quite a few evolutions and works trying to describe the main theoretical data and study. Due to the size limit and the richness of the palladium chemistry in case of experimental data, there is a great lack of computational works. In recent time, some physical and thermophysical, reaction mechanism and chemical kinetics research were been being and in views of DFT which is not enough to predict and design the new bioactive molecules and their biological properties that is why in this work, is focused on concepts and theoretical study on thermophysical, thermochemical, chemical reactivity and biological activity [15, 16].

Palladium (II) complexes currently attract considerable interest because of their potentially beneficial pharmacological properties [17, 18]. Palladium complexes have been worked against cancer cells. Although palladium has low cytotoxic effects, it has good cytotoxic effects. In this study, the palladium (II) complex was optimized with DFT/B3LYP. Some geometrical parameters, HOMO, LUMO, HOMO-LUMO gap, and LogP play the role of the chemical reactivity, biological activity [9, 12, 19]. The LogP can predict the hydrophilicity and hydrophobicity of molecule which is considered as the parameters of toxicity. The HOMO and LUMO energy level of the complex was calculated at B3LYP of DFT. On the other hand, the QSAR study can provide some useful information on biological and pharmacokinetics by which these molecules are considered as a new drug or bioactive molecule.

To design new bioactive molecules, the binuclear ligands were used which is attached with the palladium (II) ion to form different palladium (II) complex ion with binuclear ligands. The hydrazine was selected as a primary ligand and increasing one carbon atom in the next compound. Similar way, the hydrazine, 1, 2 diamino-methane, 1, 2 diamino-ethane, and 1, 2 diamino-propane ligands were used to make a comparative activity study on the basis of the alkyl chain.

Procedure for simulation

The molecular modeling program permits to build and analyze different molecular structures and determine the molecular, electronic, and biological properties. To create the spatial chemical structure of each calculated molecule, the two-dimensional structure of the molecule shall be built step-by-step by drawing. Then hydrogen atoms are automatically added from building option and chemical structure is converted into a 3D structure. The first step in getting the main characteristic parameters of molecules is to optimize the molecular structure to obtain a configuration characterized by minimum free energy. In sitting the DFT was fixed via 6G-31G*, and B3-LYP [20]. After completing optimization, the theoretical properties of the studied compound such as free energy, entropy, dipole moment, binding energy, nuclear energy, electronics energy, the heat of formation, the HOMO, LUMO are recorded. The QSAR properties of molecules such as charge density, surface area grid, volume, LogP, polarizability, refractivity, and molecular mass were calculated. The UV visible spectroscopy and IR spectroscopy were determined using the computing in vibrational optimization

Results and Discussions

Symmetry is a very powerful tool to establish the molecular symmetry calculation. In Figure 1, the palladium (II) complex ions such as L01, L02, L03, and L04 are presented of a molecular orbital diagram having both of molecular symmetry and asymmetry properties.

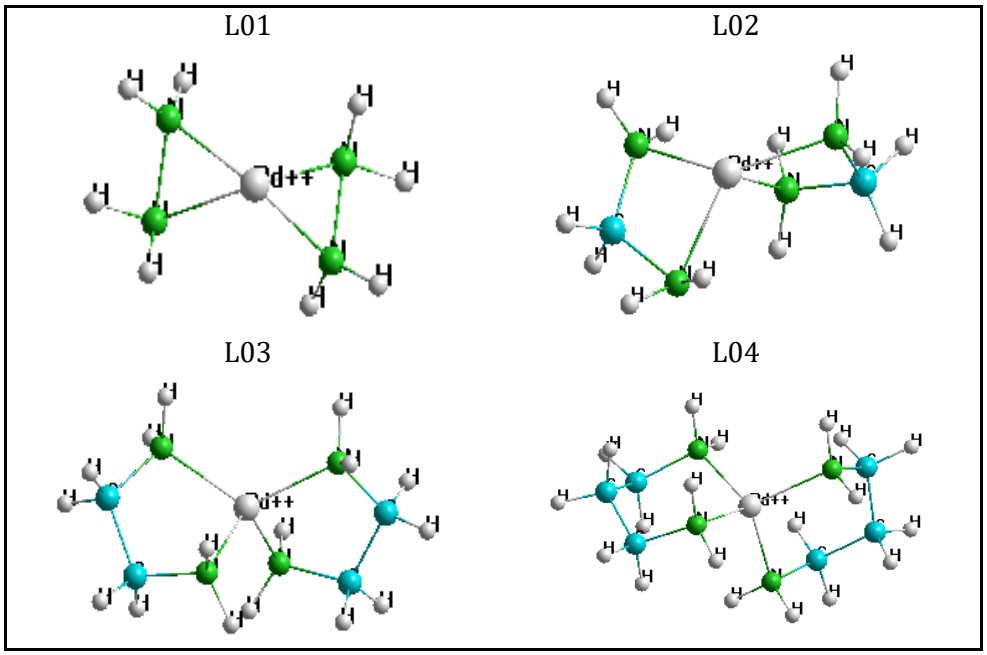
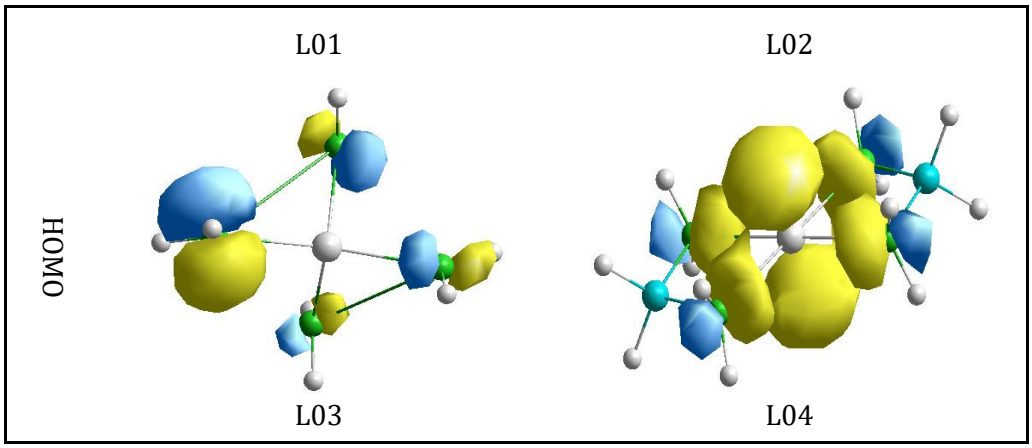


Figure 1. Optimized structure in the cylinder shape

HOMO-LUMO

The energy levels of the molecular orbitals order HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital) for palladium (II) complexes ion with different diamine ligands give information on the possible electronic transition. The HOMO and LUMO also indicated the electrophilic and nucleophilic attraction region in the molecule shown in Table 1. The LUMO-HOMO gap is the most important parameter for chemical reactivity. The shorter LUMO- HOMO gap is considered as the high reactivity, they are highlighted in Figure 2 (color: yellow is a positive value and light blue is a negative value). The values of HOMO-LUMO gap for L01, L02, L03 and L04 are 11.8486, 8.1936, 8.2712 and 8.4493, respectively. It shows that, increasing the alkyl chain decreased the HOMO-LUMO gap.



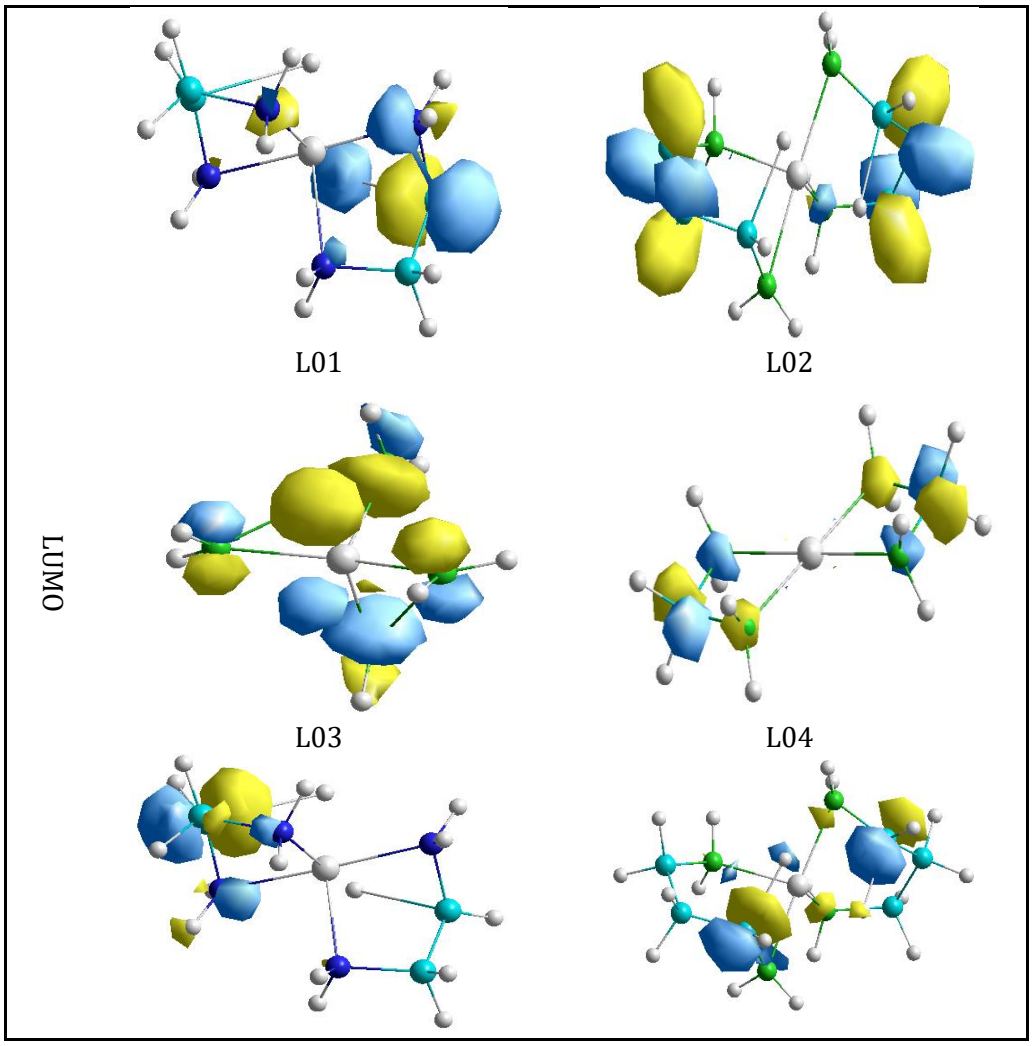


Figure 2. The frontier orbitals: a) HOMO and b) LUMO

Table 1. Data of HOMO, LUMO in different energy levels

	L01	L02	L03	L04
HOMO(0), eV	-8.2622	-4.8274	-4.2916	-4.9073
HOMO(-1), eV	3.5864	3.3662	3.9796	3.5420
HOMO(-2), eV	4.2991	4.2627	4.1991	4.4534
LUMO, (0), eV	3.5864	3.3662	3.9796	3.5420
LUMO, (-1), eV	-8.26622	-4.8274	-4.2916	-4.9073
LUMO, (-2), eV	-9.6501	-7.7879	-5.3493	-5.3396

Chemical reactivity by DFT calculations

The Energy of the HOMO is directly related to the ionization potential, and LUMO Energy is directly related to the electron affinity. The energy difference between HOMO and LUMO orbital is called an energy gap which is an important parameter that determines the stability of the structures. The energy gap is used in determining molecular electrical transport properties. In addition, according to Koopmans' theorem the energy gap, Egap,

defined as the difference between HOMO and LUMO energy and presented in Table 2 [21].

$$E_{gap} = (E_{LUMO} - E_{HOMO}) \approx IP - EA$$

The ionization potential (I) and electron affinity (A) can be estimated from the HOMO and LUMO energy values as following.

$$I = -E_{HOMO} \quad (1)$$

$$A = -E_{LUMO} \quad (2)$$

Table 2. Data for HOMO, LUMO, IP, EA, and LUMO- HOMO gap (ΔE)

	L01	L02	L03	L04
HOMO, (eV)	-8.2622	-4.8274	-4.2916	-4.9073
LUMO, (eV)	3.5864	3.3662	3.9796	3.5420
ΔE, (LUMO-HOMO) gap	11.8486	8.1936	8.2712	8.4493
Ionization potential (I),eV	8.2622	4.8274	4.2916	4.9073
Electron affinity (A),eV	-3.5864	-3.3662	-3.9796	-3.5420

The HOMO and LUMO energies are used to determine the global reactivity descriptors. It is important that electrophilicity (ω), the chemical potential (μ), electronegativity (χ), hardness (η) and softness (S) be put into a molecular orbital's framework and calculated value is listed in Table 3. We focus on the HOMO and LUMO energies in order to determine the interesting molecular properties and chemical quantities are calculated as the following equations [22].

$$(\mu) = -\frac{I+A}{2} \quad (3)$$

$$(\eta) = \frac{I-A}{2} \quad (4)$$

$$(S) = \frac{1}{\eta} \quad (5)$$

$$(\chi) = \frac{I+A}{2} \quad (6)$$

$$(\omega) = \frac{\mu^2}{2\eta} \quad (7)$$

Table 3. Biological Indices as pharmacokinetics

	L01	L02	L03	L04
Hardness, (η)	5.9263	4.0968	4.1356	4.2246
Softness, (S)	0.1687	0.2440	0.2418	0.2367
Electrophilicity (ω),	0.4209	0.0651	0.0025	0.0552
Chemical potential, (μ)	-2.3379	-0.7306	-0.1560	-0.6826
Electronegativity, (χ)	2.3379	0.7306	0.1560	0.6826

Thermophysical properties

The physical condition of any substance is known to relate to the environment of the substance and the overall condition of the substance. Various physical and chemical properties of the palladium (II) complex ion with the density functional theory were evaluated. It was found that, the change in properties can be seen by modifying the methyl group with ammonium ligand. First of all, the binding energy is accounted for methyl groups in ligand in such way that increasing the methyl groups, it is grew up, which means that the ability to connect with any of these substances increases, resulting in the form being more active as a drug. On the other hand, entropy is a property referring to the physical condition of the environment in the substance. Entropy's value increased as the stability of

the environment decreased. As seen in Table 4, all the complexes are entropy values zero, showing that their stability is almost the same. Table 5 pretends about the entropy which is raised with respect to rising temperature and with increasing methyl groups in ligand denotes the level of entropy and heat of capacity are changed with upward trends.

Table 4. Thermophysical properties

Properties	L01	L02	L03	L04
Total energy, (kcal/mol)	-48762.5718	-58196.0644	-67735.6903	-72551.6342
Entropy, (kcal/mol-deg)	0	0	0	0
Free energy, (kcal/mol)	-48762.5718	-58196.0644	-67735.6903	-72551.6343
Heat capacity, (kcal/mol-deg)	0	0	0	0.00008
Dipole moment, (D)	1.065	8.887	0	5.38
RMS gradient, (kcal/mol)	0.00009051	0.0000893	0.0015	0.000189
Binding energy, (kcal/mol)	-2186.5669	-3349.2609	-4618.0882	-5298.6328
Heat of formation, (kcal/mol)	-1227.7509	-1840.2569	-2558.8962	-2964.3468
Electronic energy, (kcal/mol)	-144659.699	-224647.0356	-305288.6746	-356862.6386
Nuclear energy, (kcal/mol)	95897.12715	166450.9712	237552.9842	28431.0044

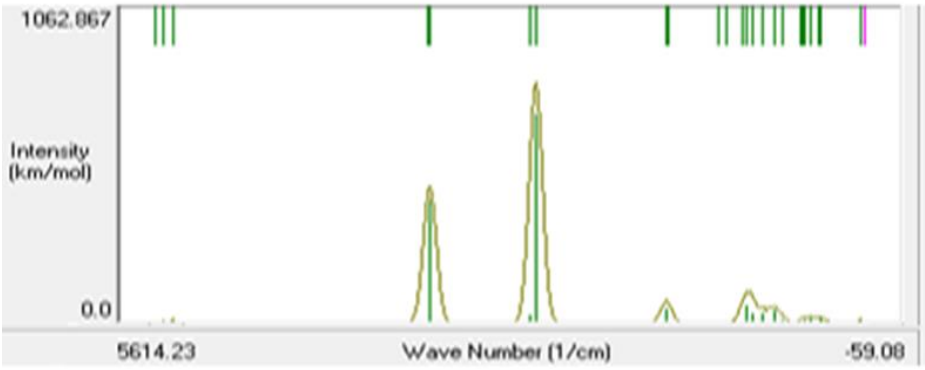
Table 5. Entropy and Heat capacity in different temperature

	273 K		298 K		323 K	
	Entropy	Heat capacity, (kcal/mol-deg)	Entropy	Heat capacity, (kcal/mol-deg)	Entropy	Heat capacity, (kcal/mol-deg)
L01	0.0741	0.0199	0.0761	0.0216	0.0781	0.0232
L02	0.0782	0.0275	0.0809	0.0304	0.0836	0.0330
L03	0.0909	0.0389	0.0946	0.0424	0.0984	0.0459
L04	0.0714	0.0094	0.0724	0.0093	0.0733	0.0097

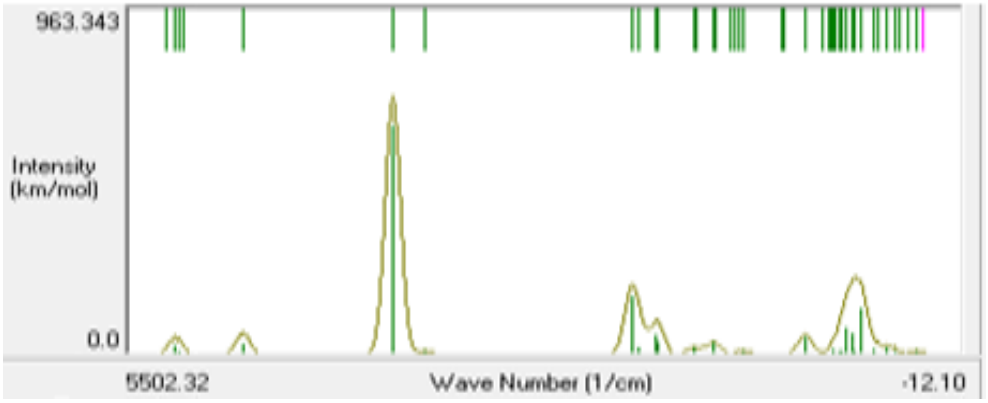
Vibrational spectrum

The vibrational spectrum is the characteristic peak of any molecule for identification similar to the FTIR peaks. To optimize these molecules for vibrational spectra, identified peak is noted in the different region about 0 to 4000 cm^{-1}. The main characteristic peak of diamine palladium (II) complex ion is almost recorded at 4000-3500, 3525-3300 and 2600-2250 cm^{-1} and represented in Figure 3 and condition in Table 6.

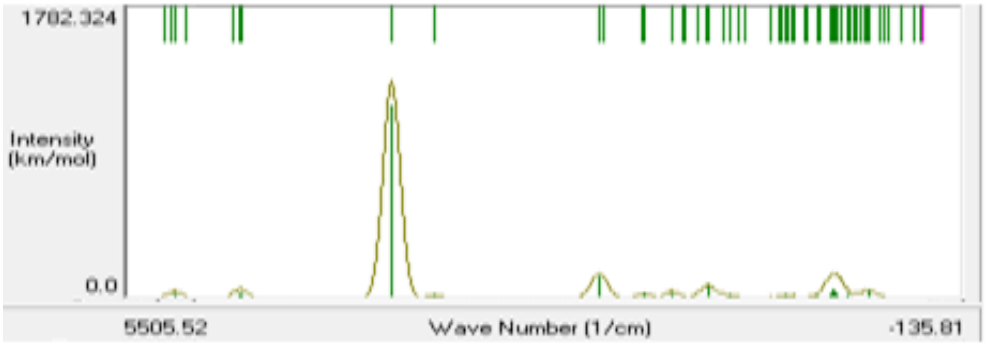
L01



L02



L03



L04

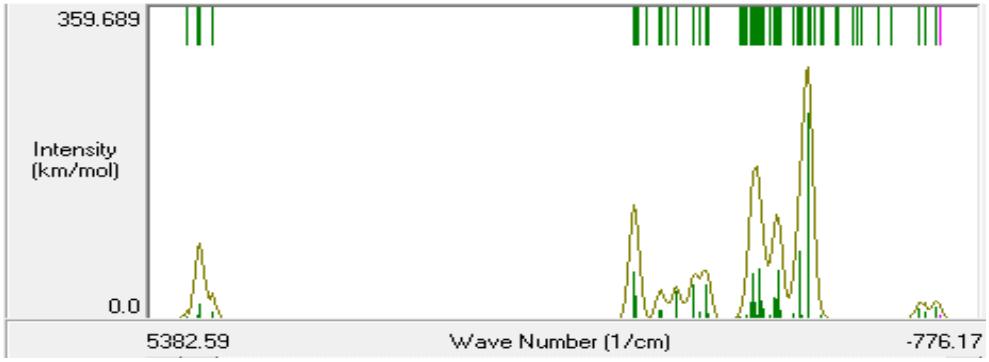


Figure 3. Vibrational spectru

Table 6. Data for a vibrational spectrum of palladium (II) complex ions

	Normal Mode	Degeneracy	Frequency	Intensity	Symmetry
L01	1	1	198.80	0.206	1 A
L02	1	1	238.56	0.266	1 A
L03	1	1	120.62	0.608	1 A
L04	1	1	-496.23	6.971	1 A

UV-visible spectrum

UV-visible spectrum provides a powerful technique by which the nature of metal-ligands bonding may be identified. A remarkable covalence between almost all of the upper filled molecular orbitals of the ligand cluster and the metal d orbitals of suitable symmetry can be calculated. The interaction between symmetry orbital like

4dxz and 4dyz for palladium metal illustrates the equality the bonding and ant-bonding levels. However, the interactions with orbitals of symmetry involve empty 4 dxy and 5 s metal orbitals, result in important ligand-to-metal charge transfer [23]. The UV-visible spectrum of the diamine palladium (II) complex ion shows a strong transition near 135 and 170-180 nm, as well as an ultraviolet band of weaker intensity after 250 nm (Figure 4 and Table 7.

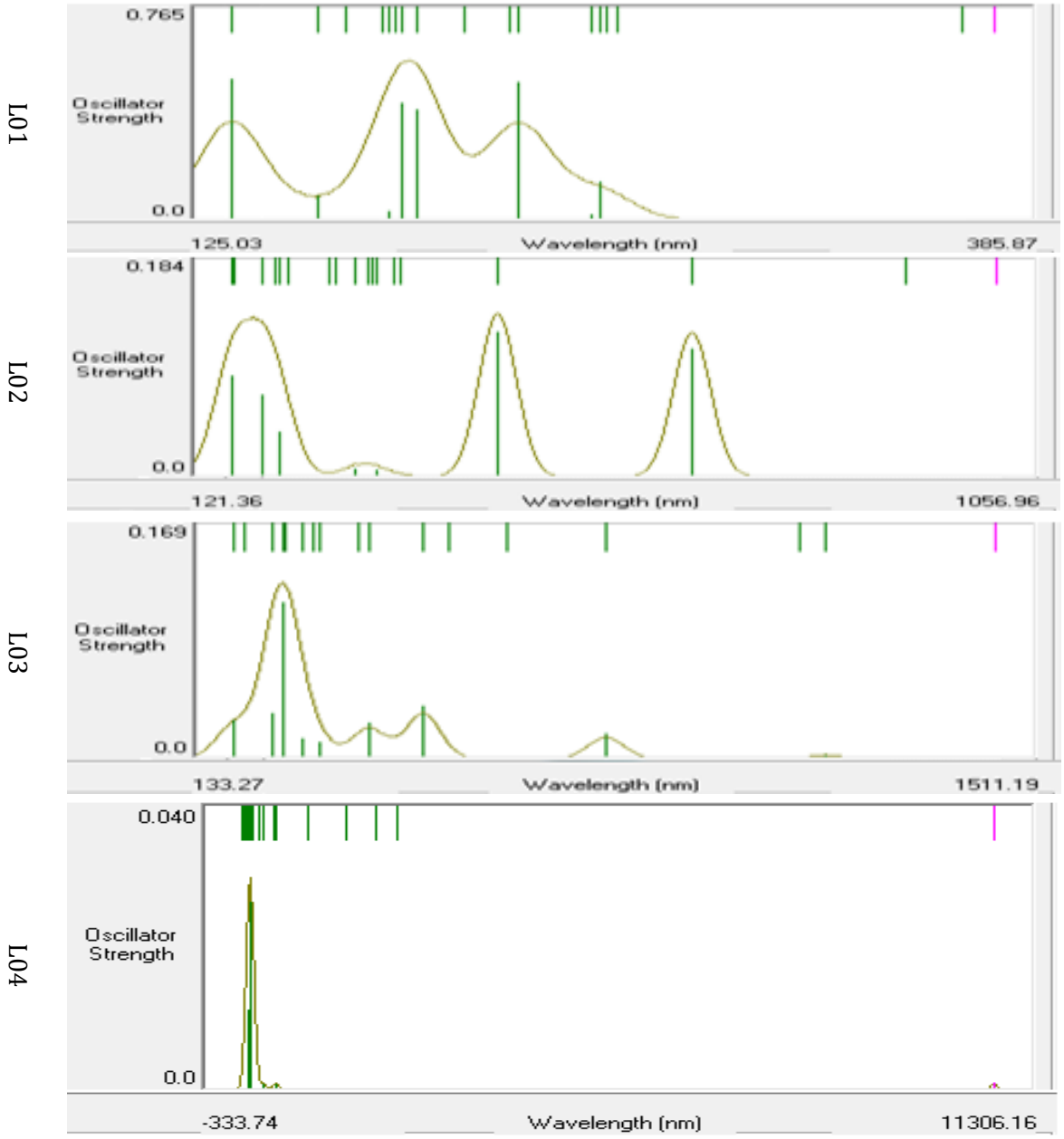


Figure 4. UV-visible Spectrum

Table 7. Data for different transition state, spin multiplicity, wavelength and oscillator strength for UV –visible spectrum

	Transition	Degeneracy	Spin Multiplicity	Wavelength	Oscillator Strength
L01	1	1	Triplet	374.01	0.0
L02	1	1	Triplet	1014.43	0.0
L03	1	1	Triplet	1448.56	0.0
L04	1	1	Triplet	10777.07	0.0

Biological activity of optimized molecules

Distribution electrostatic potential due to 3d mapped structure

The electrostatic potential is an important property through which it can be easily detected by a different charge distribution over molecule. Increasing the amount of charge in a single molecule will increase the same biological activity. The three-dimensional geometry of molecular electrostatic potential distribution highlights the existence of three regions with increased electronegativity in the whole molecule of L01, L02 and highly positivity in L03 and L04 (shown in Figure 5 and Table 8), playing an important role in their coupling to different structures in which ions are positively charged

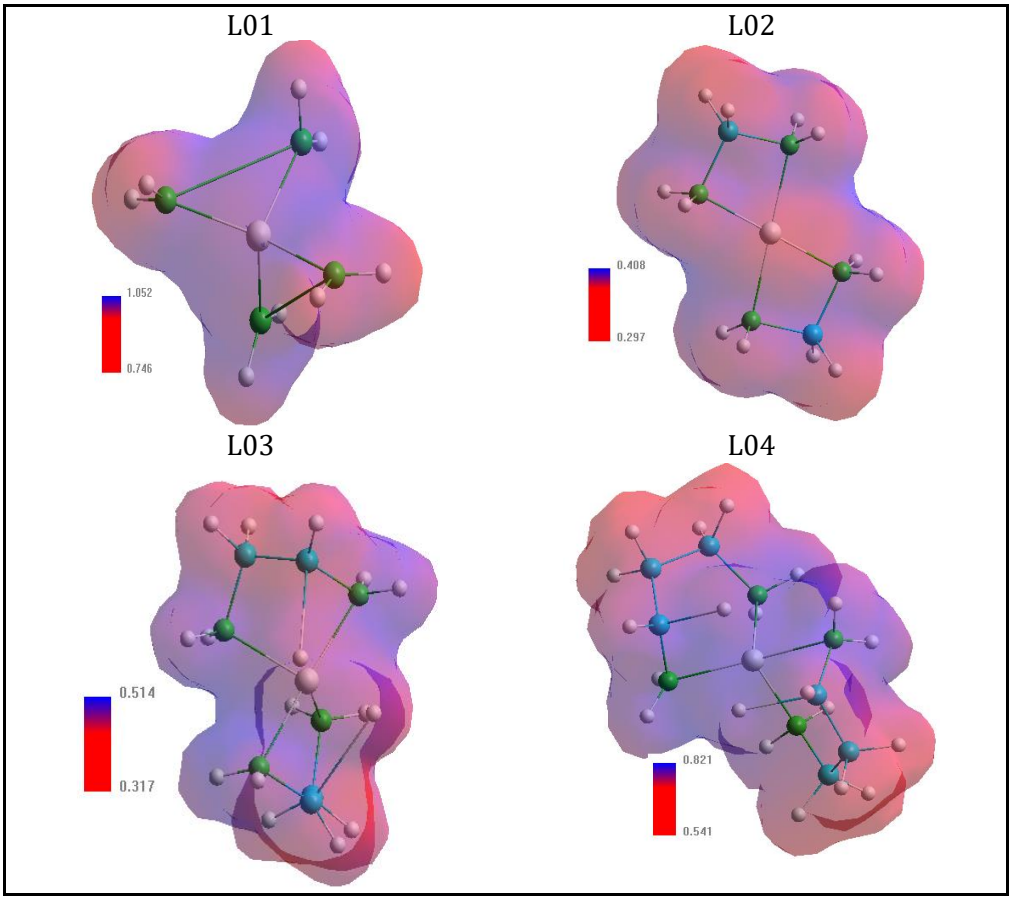


Figure 5. The 3D geometry of the distribution electrostatic potential

Table 8. Data of electrostatic potential energy difference of two levels

	L01	L02	L03	L04
E1	1.052	0.408	0.514	0.821
E2	0.746	0.297	0.317	0.541
ΔE= E2-E1	-0.306	-0.111	-0.197	-0.280
Total Charge Density contour value	0.05	0.05	0.05	0.05

Here, E1=Electrostatic potential energy in positive value, E2=Electrostatic potential energy in negative value and ΔE=Electrostatic potential energy difference of two level.

Quantitative structure-activity relationships (QSAR)

Some of the key parameters of QSAR analysis are LogP, refractivity, hydration energy, and molecular mass, through which analyzed complexes are determined by bio-activities. Surface area is a physical property of the substance that has a special role in the biological activity. Also, increasing the surface area enhanced the biological property of the molecules. On the other hand, a negative value of logP indicated the hydrophilicity and positive LogP indicated the hydrophobicity that plays an important role in biochemical interactions and bioactivity. Hydrophobic drugs tend to be more toxic due to a wider distribution in the body and less selective in their binding to molecules.

Finally, the correlation of L01, L02, L03, and L04 complexes ion are increased the biological activity as increasing the size of ligands with fine correlation (Table 9).

Table 9. Data for QSAR study

	L01	L02	L03	L04
Partial charge, (e)	0.00	0.00	0.00	0.00
Surface Area(grid),	245.64	276.41	320.51	335.07
Volume, Å^3	327.02	390.90	484.95	510.60
Hydration Energy kcal/mol	-31.37	-11.93	-8.92	-10.93
Log P	-2.61	-2.55	-3.28	-3.23
Refractivity Å^3	6.40	14.87	25.25	30.11
Polarizibility, Å^3	3.19	6.86	10.53	12.37
Mass (amu)	170.49	198.54	226.60	240.62

The correlation between the biological activity and descriptor was developed by Zineb Almi *et al.* [24] for the PIC50 value calculation from the Hyperchem simulation value that is given in the following equation (Table 10)

$$PIC50 = 3.028 - 0.542logP + 0.352\ HE - 1.272\ Pol + 0.863MR - 0.038\ MV - 0.024MW + 19.120q01 + 0.024SAG \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 08$$

Here, HE=Hydration energy, Pol= Polazibility, MR=Molecular refractivity, Log P= Partition coefficient, MV=Molar volume, MW=Molar weight, SAG=surface area grid, q01=atomic net charges.

Table 10. Data of PIC50

	L01	L02	L03	L04
PIC50	-15.757	-13.128	-6.111	-5.955

Correlation and comparison study in case of substituent groups in amine ligands

In the case of chemical reactivity from Figure 6, the LUMO-HOMO gap at the presence of L02, L03, and L04 is almost the same means that with increasing alkyl chain with the nitrogen atom in ligands, the chemical reactivity is changed poorly. However, the chemical reactivity in hydrazine is lower than the others, showing that attaching carbon chain with nitrogen atom has higher reactivity.

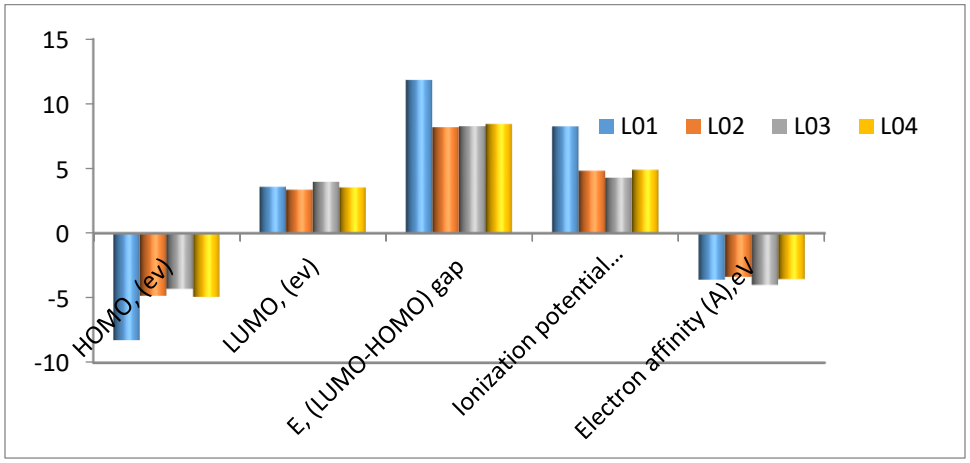


Figure 6. Comparison of chemical reactivity of palladium (II) complex ion with binuclear amine ligands

By increasing the carbon chain in nitrogen atom of ligands, the total energy, binding energy, free energy, heat of formation, and electronics energy were increased (Figure 7).

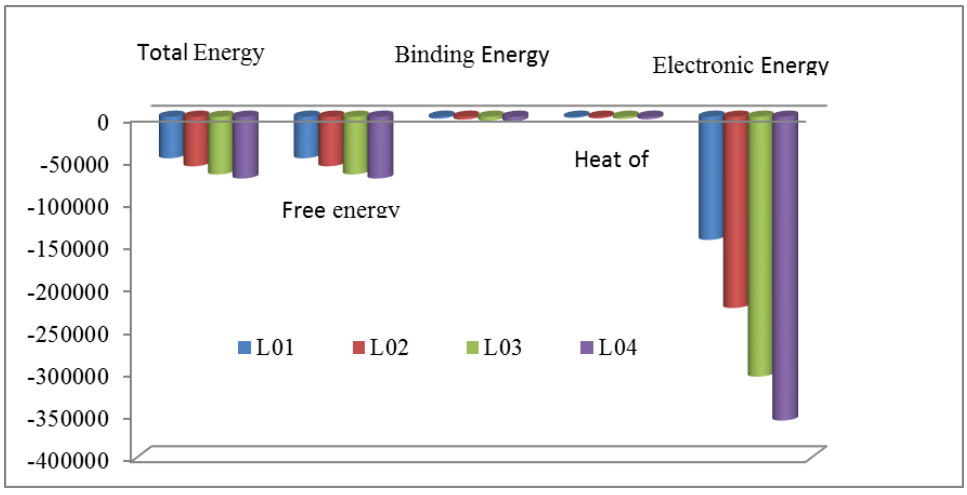


Figure 7. Comparison of thermophysical properties of palladium (II) complex ion with binuclear amine ligands

As seen in Figure 8, the attaching of carbon chain in amine ligand had higher surface area, volume, and molecular mass, showing that the biological activity was increased.

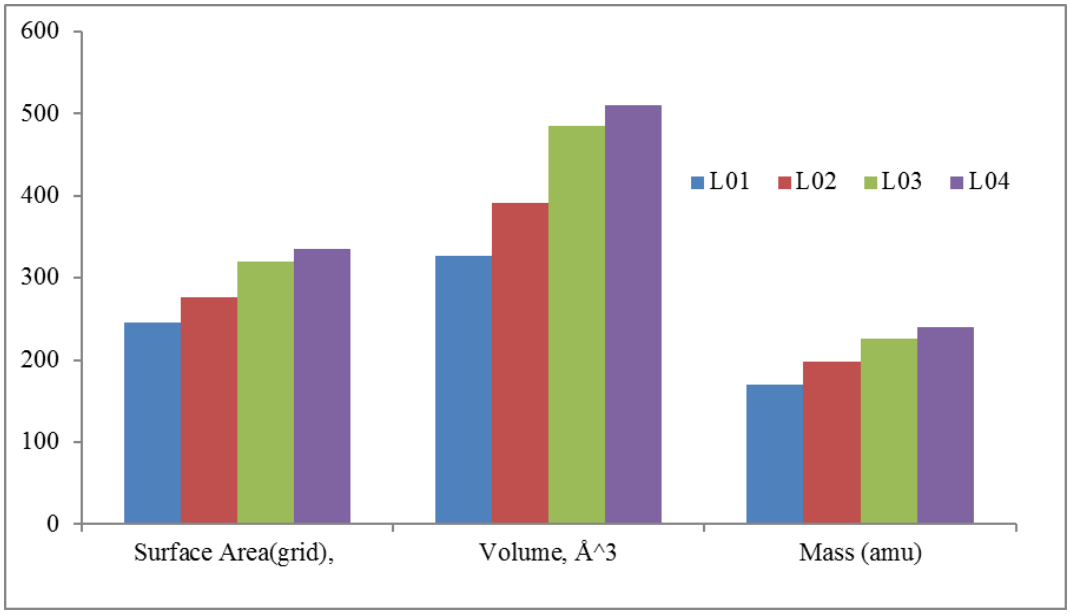


Figure 8. Comparison of biological activity of palladium (II) complex ion with binuclear amine ligands

In case of QSAR study, the PIC50 value of L04 and L03 is -5.955 and -6.111, indicating the highly biological active molecules. The L01 and L02 have the PIC50 -15.757 and -13.128, showing that lower biological activity. From the data of LogP, all molecules pose the negative value and is regarded as hydrophilic nature and tend to no toxicity**.** By increasing the alkyl chain in nitrogen atom of ligands, the toxicity decreased (Figure 9).

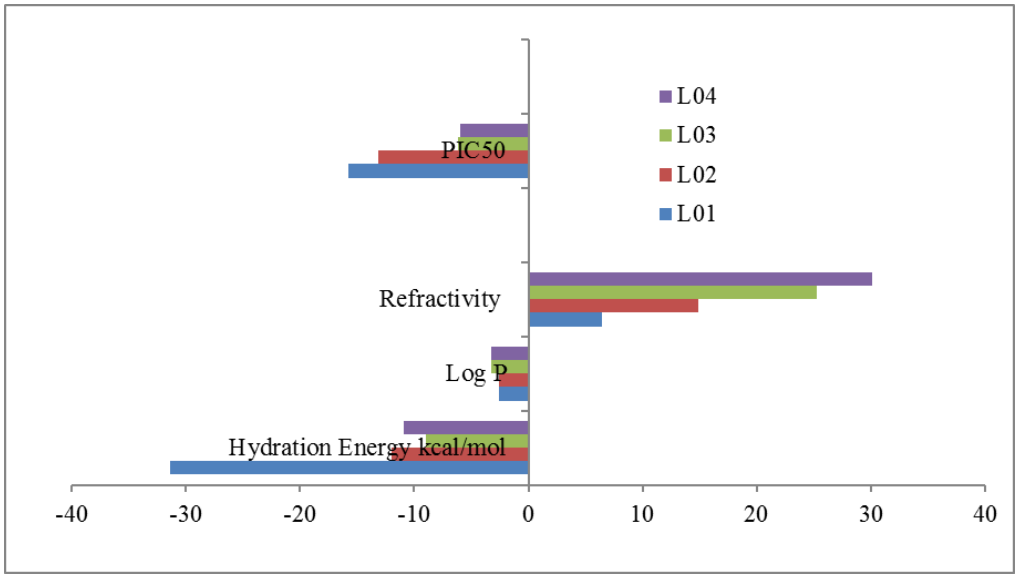


Figure 9. Comparison of QSAR study of palladium (II) complex ion with binuclear amine ligand

Conclusion

In this research study, the DFT method was used to characterize and optimize the palladium (II) complex ions with binuclear amine ligands and the thermophysical and chemical and biological properties were recorded. The vibration, degeneracy, symmetry, and splitting of d orbitals provided information in the analytical method. In the case of HOMO, LUMO, and HOMO–LUMO gap can be informed that palladium (II) complex ions with binuclear amine ligands are chemically reactive for further uses. As the value of LogP was negative, palladium (II) complex ions with binuclear amine ligands are hydrophilic nature. This is why the toxicity was very low, supporting the safe uses in all areas

Disclosure Statement

No potential conflict of interest was reported by the authors.

Orcid

Mohammad Jahidul Islam 0000-0002-4125-8222

Sunanda Paul 0000-0001-7739-4018

Ajoy Kumer 0000-0001-5136-6166

Md. Nuruzzaman Sarker 0000-0003-2760-0113

References

[1]. Chen X., Engle K.M., Wang D.H., Yu J.Q. *Angewandte Chemie International Edition*, 2009, **48**:5094

[2]. Lazarević T.R., Bugarčić A., Živadin D. *European journal of medicinal chemistry*, 2017, **142**:8

[3]. Ray S.M., Singh R., Jay K., Samantaray Manoja K., Shaikh Mobin M., Panda D., Ghosh P. *Journal of the American Chemical Society*, 2007, **129**:15042

[4]. Ajoy Kumer M.N.S., Sunanda PAUL, *International Journal of Chemistry and Technology*, 2019, **3**:26

[5]. Ajoy Kumer M.N.S., Paul S., Zannat A. *Advanced Journal of Chemistry-Section A*, 2019, **2**:190

[6]. Islam M.J., Sarker Md.N., Kumer A., Paul S. *International journal of Advanced Biological and Biomedical Research*, 2019, **7**:318

[7]. Islam M.J., Kumer A., Sarker Md. N., Paul S., Zannat A. *Advanced Journal of Chemistry-Section A*, 2019, **2**:316

[8]. Ajoy K., Paul S., Sarker Md.N., Islam M.J. *International Journal of New Chemistry*, 2019, **6**:236

[9]. Ajoy K., Sarker Md.N., Pual S. *Eurasian Journal of Environmental Research*, 2019, **3**:1

[10]. Islam M.J., Sarker Md.N., Kumer A., Paul S., *International journal of Advanced Biological and Biomedical Research*, 2019, **7**:306

[11]. Kumer A., Ahmed B., Sharif Md.A., Al-Mamun A. *Asian Journal of Physical and Chemical Science*, 2017, **4**:1

[12]. Sarker Md.N., Ajoy K., Islam M.J., Sunanda P. *Asian Journal of Nanoscience and Materials*, 2019, **2**:439

[13]. Miyaura N., Suzuki A. *Chemical eviews*, 1995, **95**:2457

[14]. Miyaura N., Yanagi T., Suzuki A. *Synthetic Communications,* 1981, **11**:513

[15]. Hossain M.I., Ajoy K. *Asian Journal of Chemical Science*, 2018, **3**:1

[16]. Kumer A., Ahmed B., Sharif M.A., Al-Mamun A. *Asian Journal of Physical and Chemical Science*, 2017, **4**:1

[17]. Garrett C.E., Prasad K. *Advanced Synthesis & Catalysis*, 2004, **346**:889

[18]. Doucet H., Hierso J.C. *Current opinion in drug discovery & development*, 2007, **10**:672

[19]. Ajoy K., Sunanda P., Sarker N.Md., Islam

J.M. *International Journal of New Chemistry*, 2019, **6**:236
[20]. Howard A., McIver J., Collins J. Hyperchem computational chemistry. *Hypercube Inc*., Waterloo 1994
[21]. Koopmans Y.T. *Physica*, 1934, **1**:104
[22]. Parr R.G., Szentpály L.V., Liu S. *Journal of the American Chemical Society*, 1999, **121**:1922
[23]. Canadell S., Pouget J.P., Brossard L. *Solid State Communications*, 1990, **75**:633
[24]. Zineb Almi S.B., Lanez T., Tchouar N. *International Letters of Chemistry, Physics and Astronomy*, 2014, **37**:113

How to cite this manuscript: Mohammad Jahidul Islam, Sunanda Paul, Ajoy Kumer*, Md. Nuruzzaman Sarker, Computational approach of palladium (II) complex ions with binuclear diamine ligands thermo-physical, chemical, and biological properties: a dft study. *Journal of Medicinal and Nanomaterials Chemistry*, 2(1), 2020, 67-81. DOI: 10.48309/JMNC.2020.1.7