Some Molecular Properties and Reaction Mechanism of Synthesized Isatin Thiosemicarbazone and Its Zinc(II) and Nickel(II) Complexes

Fatma Kandemirli¹, Can Dogan Vurdu¹, Murat Saracoglu²*, Yusuf Akkaya³ and Muhammet Serdar Çavuş¹

¹Biomedical Engineering Department, Faculty of Engineering and Architecture, Kastamonu University, Kastamonu, Turkey.
²Faculty of Education, Erciyes University, Kayseri, Turkey.
³Department of Chemistry, Faculty of Science, Nigde University, Nigde, Turkey.

Authors’ contributions

This work was carried out in collaboration between all the authors. Author FK designed the study and wrote the protocol, executed the work and interpreted the results. Author YA executed the work, managed literature searches, and author MS fashioned the second draft of the manuscript, managed literature searches. Authors CDV and MSC wrote the protocol and interpreted the results managed literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IRJPAC/2015/17626

Editor(s):
(1) Sung Cheal Moon, Korea Institute of Materials Science (KIMS), Industrial Technology Support Division, Changwon, Republic of Korea.

Reviewers:
(1) Anonymous, National University of Mongolia, Mongolia.
(2) Michaela Filipi, University of Pardubice, Czech Republic.
(3) Anonymous, University of Kragujevac, Serbia.
(4) Anonymous, Wroclaw University of Technology, Poland.

Complete Peer review History: http://sciencedomain.org/review-history/9763

Received 20th March 2015
Accepted 19th May 2015
Published 15th June 2015

ABSTRACT

The aim of this study is to 1H-Indole-2,3-dione 3-[N-(4-fluorophenyl)-thiosemicarbazone and its zinc(II) and nickel(II) complexes. The structures of the synthesized compounds were confirmed by spectral data and elemental analysis. They were optimized by B3LYP theory with different basis sets. The optimized structures were compared with the experimental values. TD-DFT calculations

*Corresponding author: E-mail: muratsaracoglu@gmail.com;
on electronic absorption spectra in gas phase and DMSO were performed to determine the electronic transitions of the compounds. The Frontier Molecular Orbital analysis were also done in order to identify the charge transfer interaction that takes place between the molecular orbitals. Reaction mechanism of 1H-indole-2,3-dione-3-(N-4-fluorophenyl thiosemicarbazone) molecules were also studied.

Keywords: Isatin; metal complexes; thiosemicarbazone; chemical computational calculations.

1. INTRODUCTION

Isatin thiosemicarbazones are the most important class of biologically active ligands providing potential binding sites through nitrogen and sulphur donor atoms belonging to thiosemicarbazone group and oxygen donor atoms belong to indole ring [1-5]. Metal complexes of isatin thiosemicarbazone derivatives, especially Zn(II), Ni(II), Pd(II) and Pt(II), have been extensively synthesized by several researchers because of their biological active properties, such as antibacterial, antiviral, anti-tuberculosis, antifungal activities [6-11].

We have recently experimentally synthesized and characterized some isatin thiosemicarbazones complexes, such as 5-methoxy and 5-fluoro isatin thiosemicarbazone, and theoretically studied the quantum chemical properties [12-18].

In this study, the theoretical vibrational spectrum, UV spectrum, $^{13}$C and $^1$H NMR values, molecular polarizability, molecular geometry, and atomic charges have been performed for 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone and its zinc(II) and nickel(II) complexes by using B3LYP hybrid functional with basis sets, 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p) and 6-311++G(2d,2p). Fukui functions have been calculated by using AOMix [16-17] from single-point calculations with B3LYP/6-311G(d,p).

2. MATERIALS AND METHODS

2.1 Experimental

Synthesis of 1H-indole-2,3-dione 3-[N-(4-fluorophenyl)-thiosemicarbazone]-I4FPTH$_2$ was carried out by stirring 0.294 g (2 mmol) of isatin in 75 mL ethanol on a hot plate magnetic stirrer until dissolved and adding 0.306 g (2 mmol) of 4-florophenyl-3-thiosemicarbazide dissolved in ethanol and about 2-3 drops of fuming sulphuric acid on isatin solution under stirring, respectively. The mixture was refluxed for about 2-3 hours. The precipitated product was filtered, purified and dried. Orange solid product was obtained.

C$_{15}$H$_{11}$ON$_2$S (Melting point, MP: 240.9°C and Molecule weight, MW=314.34 g/mol), IR(cm$^{-1}$): 3293, 3174(NH), 1684(C=O), 1621(C=N), 867(C=S), $^1$H NMR(dmso-d$_6$,ppm): 7.74(dd, 1H, indol-C$_2$-H), 7.58(dd, 2H, phenyl), 7.35(dt, 1H, indol-C$_5$-H), 7.27(dd, 2H, phenyl), 7.13(dt, 1H, indol-C$_6$-H), 6.92(dd, 1H, indol-C$_7$-H), 10.83(t, 1H, N$_2$-H), 11.26(s, 1H, indol-NH), 12.80(s, 1H, N$_2$-H). (Calc.: C, 57.31; H, 3.53; N, 17.82; S, 10.20%; Found: C, 55.78; H, 2.96; N, 17.43; S, 10.93%).

2.1.1 Synthesis of bis(1H-indole-2,3-dione 3-[N-(4-fluorophenyl)thiosemicarbazone]Zn(II)-Zn[[I4FPTH]$_2$]

0.3142 g (1 mmol) of I4FPTH$_2$ was dissolved in 20 mL methanol at about 50-55°C and then 0.1097 g (0.5 mmol) of zinc acetate tetrahydrate dissolved in 15 mL methanol was slowly added on it to synthesize the Zn[[I4FPTH]$_2$] complex. The mixture was refluxed for about 6-9 hours. A dark orange product was obtained. The Zn[[I4FPTH]$_2$] complex was washed with ethanol and diethyl ether, and then dried (MP: 256°C). (Calc.: C, 52.07; H, 2.91; N, 16.19; S, 8.98%; Found: C, 51.66; H, 2.92; N, 15.91; S, 8.98%).

2.1.2 Synthesis of bis(1H-indole-2,3-dione 3-[N-(4-fluorophenyl)thiosemicarbazone]Ni(II)-Ni[[I4FPTH]$_2$]

Ni[[I4FPTH]$_2$] complex was synthesized by dissolving 0.3142 g (1 mmol) of I4FPTH$_2$ in 20 mL of methanol at about 50-55°C and then slowly adding 15 mL methanol solution containing 0.1244 g (0.5 mmol) of nickel acetate tetrahydrate. The mixture was refluxed for about 2 hours. Brown Ni[[I4FPTH]$_2$] complex was precipitated, washed with ethanol and diethyl ether, and then dried (MP: 258°C). (Calc.: C, 52.57; H, 2.94; N, 15.91; S, 9.35%; Found: C, 50.94; H, 2.90; N, 15.60; S, 8.67%).
2.2 Calculation Method

I4FPTH$_2$ ligand was optimized at the level of B3LYP theory with 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311G(2d,2p) basis sets, and Zn[(I4FPTH)$_2$], Ni[(I4FPTH)$_2$] complexes were optimized at the level of B3LYP theory with 6-31G(d,p), 6-311G(d,p) basis sets in gas phase and DMSO solvent. $^1$H and $^{13}$C NMR chemical shifts were calculated by using the GIAO method at the level of B3LYP theory with 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311G(2d,2p) basis sets for I4FPTH$_2$ ligand. Reaction mechanism of I4FPTH$_2$ ligand was performed with semi-empirical method by using AM1 Package program. Gaussian 09 was used to perform calculations [19].

3. RESULTS AND DISCUSSION

Fig. 1 shows the optimized structure of 1H-indole-2,3-dione 3-[N-(4-fluorophenyl)]thiosemicarbazone molecules with the atom numbering calculated by using B3LYP/6-311G(d,p). Calculated bond lengths of I4FPTH$_2$ molecule with B3LYP/6-31G(d,p), B3LYP/6-311G(d,p), B3LYP/6-311++G(d,p), B3LYP/6-311G(2d,2p) method in gas phase and DMSO solvent are given in Fig. 2 and Mulliken charges are presented in Fig. 3.

![Fig. 1. The optimized structure of 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone molecules with the atom numbering calculated by using B3LYP/6-311G(d,p)](image)

![Fig. 2. Bond lengths of 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone molecules](image)
It was observed that there was negative charge density on C17, C11, C5, C4, N6, O9, N21, N20, S7, N19 atoms in both gas and liquid (DMSO) phase. Calculations were completed by using B3LYP method and 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311G(2d,2p) basis sets for I4FPTH$_2$. Charge densities vary in accordance with the basis sets and depending on whether the gas or liquid phases. Mulliken charge of C17 atom calculated with the 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311G(2d,2p) basis sets are -0.125, -0.027, -0.330, -0.302 ē, respectively in gas phase, while in DMSO are -0.148, -0.051, -0.351, -0.315 ē and for N21 atom in gas phase are -0.380, -0.240, -0.068, -0.373 ē while in DMSO -0.386, -0.241, -0.082, -0.396 ē.

The optimized structures for the Zn[([4FPTH])$_2$] and Ni([4FPTH])$_2$ complexes calculated according to B3LYP/6-311G(d,p) level are given in Fig. 4. Bond lengths calculated with the B3LYP level and 6-311G(d,p) 6-31G(d,p), 6-311G(d,p) basis sets are given in Fig. 5 and Mulliken charges are given in Fig. 6. As can be seen from the Fig. 5, there is no significant difference in bond lengths according to the basis sets. Therefore, either 6-311G(d,p), or 6-311G(d,p) basis sets might be preferred to calculate bond lengths.

Bond lengths of I4FPTH$_2$ ligand, Zn([4FPTH])$_2$ and Ni([4FPTH])$_2$ complexes calculated according to B3LYP/6-311G(d,p) theory are given in Fig. 7. Bond length for C15-C17 atoms belong to indole ring for I4FPTH$_2$ ligand, Zn([4FPTH])$_2$ and Ni([4FPTH])$_2$ complexes is 1.390, 1.393, 1.395 Å; for C10-N6 bond length is 1.403, 1.396, 1.392 Å; for C18-N21 bond length is 1.296, 1.305, 1.310 Å and for N21-N20 bond length is 1.332, 1.357, 1.347 Å, respectively. There is a little increasing in bond lengths at thiosemicarbazone side of complexes.

Negative charge density on C11, C5, C4, N6, O9 atoms and positive charge density on C10, C12, C18 atoms belong to indole ring of Zn([4FPTH])$_2$ complex was found. The negative charge density on C11, C5, C4, N6, O9 atoms are -0.106 ē, -0.092, -0.108 ē, -0.674 ē, -0.476 ē for 6-31G(d,p) basis set and 0.034, -0.135, -0.083, -0.048, -0.490, -0.316 ē for 6-311G(d,p) basis set, respectively. The positive charge density on C10, C12, C18 atoms are 0.304, 0.622, 0.261 ē for 6-31G(d,p) basis set and 0.252, 0.429, 0.204 ē for 6-311G(d,p) basis set, respectively. N21, N20, S7, N19 atoms belong to thiosemicarbazone group have negative charge density, these are 0.499, -0.227, -0.598 ē for 6-31G(d,p) basis set, and -0.533, -0.220, -0.436, -0.399 ē for 6-311G(d,p) basis set, respectively. Mulliken charge calculated with 6-311G(d,p) is lower than of 6-31G(d,p).

According to B3LYP/6-311G(d,p) theory; the Mulliken charges on C17, C11, C5, C4, C10, C18 atoms belong to indole ring are -0.125, -0.027, -0.330, -0.302 ē, respectively in gas phase, while in DMSO are -0.148, -0.051, -0.351, -0.315 ē and for N21 atom in gas phase are -0.380, -0.240, -0.068, -0.373 ē while in DMSO -0.386, -0.241, -0.082, -0.396 ē.
C15, N6, C12, O9, C18 atoms are -0.027, -0.100, -0.090, -0.041, 0.239, -0.135, -0.489, 0.422 ē, for I4FPTH$_2$ ligand; 0.034, -0.135, -0.083, -0.048, 0.252, -0.157, -0.490, 0.429, -0.316, 0.204 ē, for Zn[(I4FPTH)$_2$] complex and 0.012, -0.113, -0.082, -0.051, 0.239, -0.132, -0.488, 0.239, -0.132, 0.224 ē, for Ni[(I4FPTH)$_2$] complex, respectively. Mulliken charges on N21, N20, C16, S7, N19, C13 belong to thiosemicarbazone group are -0.240, -0.270, 0.230, -0.214, -0.462, 0.199 ē, for I4FPTH$_2$ ligand; -0.533, -0.220, 0.164, -0.436, -0.399, 0.143 ē, for Zn[(I4FPTH)$_2$] complex and -0.485, -0.263, 0.195, -0.312, -0.428, 0.169 ē, for Ni[(I4FPTH)$_2$] complex, respectively. Mulliken charge of Zn atom in Zn[(I4FPTH)$_2$] complex and Ni atom in Ni[(I4FPTH)$_2$] complex were calculated as 1.379 and 1.045 ē (Fig. 8).

**Fig. 4.** Optimized structure of Zn[(I4FPTH)$_2$] and Ni[(I4FPTH)$_2$]

**Fig. 5.** Bond lengths for (a) Zn[(I4FPTH)$_2$] and (b) Ni[(I4FPTH)$_2$] complexes
Fig. 6. Mulliken charges for Zn[(I4FPTH)_2] and Ni[(I4FPTH)_2] complexes

Fig. 7. Bond lengths for I4FPTH$_2$, Zn[(I4FPTH)$_2$] and Ni[(I4FPTH)$_2$] calculated with B3LYP/6-311G(d,p) method
3.1 Reaction Mechanism Study of 1H-indole-2,3-dione-3-(N-4-fluorophenyl thiosemicarbazone) Molecules

The calculation was carried out on protonated form of 1H-indole-2,3-dione and 4-(4-Fluorophenyl)-3-thiosemicarbazide and continued to protonated form of product in the reaction mechanism study. The reaction mechanism was studied with semi-empirical method Austin Model (AM1). Reactants, transition states (TS), intermediates (IN1) and products of spatial arrangements of atoms are given in Fig. 9. Bond lengths and Mulliken charges of 1a-2, TS1, IN1, TS2, 3b molecules are given in Fig. 10.

Gaussian assumes electronic distribution as a function of the molecular geometry (Born-Oppenheimer approximation). The vibrational frequency calculations are required for understanding whether it has been obtained from a stable minimum structure. Negative imaginary frequencies were found in calculations for TS1 and TS2 (the negative frequencies for TS1 and TS2 are 315 and 1743 cm⁻¹).

As well as the presence of a negative frequency defining the minima connected through the transition state is required. We chose the intrinsic reaction coordinate (IRC), and defined as the minimum energy reaction pathway (MERP) in mass-weighted Cartesian coordinates that between the transition state of a reaction and its reactants and products (Fig. 11).

4-(4-Fluorophenyl)-3-thiosemicarbazide molecule and protonated 1H-indole-2,3-dione molecule are far from each other (C13-N17= 3.00 Å). The distance between N17 atom belong to 34-(4-Fluorophenyl)-3-thiosemicarbazide molecule and C13 atom attached to protonated 1H-indole-2,3-dione molecule in the transition state, intermediate state and product state is 1.950, 1.496, 1.560, 1.314 Å, respectively. C=O bond length belong to indole ring in reactant state, TS1, IN, TS2 and product state is found as 1.226, 1.229, 1.230, 1.232 and 1.226 Å, respectively. The Mulliken charge of N17 atom in reactant state, TS1, IN, TS2 and product state is 0.290, -0.235, -0.001, -0.052, -0.025 ė, respectively and the Mulliken charge of C11 atom in reactant state is 0.276, 0.299, 0.144, 0.107, 0.144 ė, respectively. This explains that, N17 atom belong to 4-(4-Fluorophenyl)-3-thiosemicarbazide molecule attacks to C13 atom attached to protonated 1H-indole-2,3-dione ring as nucleophile.

The reactivity of a molecule is closely related to the highest occupied molecular orbital-HOMO and the lowest empty molecular orbital –LUMO and the parameters such as hardness, softness can be calculated using HOMO and LUMO energies. The higher value of $E_{\text{HOMO}}$ means its ability to donate electrons to appropriate
acceptor molecules with low energy empty MO. \(E_{\text{HOMO}}\) value indicates the ability to donate electrons and \(E_{\text{LUMO}}\) indicates the ability to accept electrons. HOMO, LUMO energies and five molecular orbital energies close to HOMO and LUMO of \(\text{I}4\text{FPTH}_2\) molecule obtained from the calculations with the 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311G(2d,2p) basis sets of B3LYP method in gas phase and solvent (DMSO) (Fig. 12) and those for Zn(\([\text{I}4\text{FPTH})_2]$, Ni(\([\text{I}4\text{FPTH})_2]$ calculated with the 6-31G(d,p), 6-311G(d,p) basis sets of B3LYP method are given in Fig. 13.

It was observed that \(E_{\text{HOMO}}\) and \(E_{\text{LUMO}}\) values calculated with B3LYP method for carried out basis sets in DMSO solvent were lower than those in gas phase. For example, while \(E_{\text{HOMO}}\) values in the gas phase calculations by using 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311G(2d,2p) basis sets are -0.21723, -0.22651, -0.23083, -0.22967 au, in the DMSO solvent calculations are -0.22080, -0.22847, -0.23206, -0.23073 au. \(E_{\text{LUMO}}\) values are -0.09713, -0.10535, -0.11099, -0.10979 au in gas phase, and -0.09283, -0.10157, -0.10648, -0.10528 au in DMSO solvent.

HOMO and LUMO energies for Zn(\([\text{I}4\text{FPTH})_2]$, Ni(\([\text{I}4\text{FPTH})_2]$ calculated with 6-31G(d,p) basis set is higher than those calculated with 6-311G(d,p) basis set. HOMO with the 5 molecular orbital energies close to Frontier orbitals and LUMO with the 5 molecular orbital energies close to Frontier orbitals are -0.20833, -0.20901, -0.21880, -0.22292, -0.23609, -0.23976, -0.10223, -0.10212, -0.01576, -0.00909, -0.00879 au for the calculations with 6-31G(d,p), 6-311G(d,p) basis sets of B3LYP method (Fig. 13).

Frontier orbital energies of ligand and its zinc(II) and nickel(II) complexes are given in Fig. 14. HOMO energy for \(\text{I}4\text{FPTH}_2\) ligand and Zn(\([\text{I}4\text{FPTH})_2]$, Ni(\([\text{I}4\text{FPTH})_2]$ complexes at the level of theory B3LYP/6-31G(d,p) were calculated as -0.22651, 0.19795, -0.21823 au, respectively and LUMO energies of those were calculated as -0.09283, -0.00879, -0.10979 au. HOMO energies of complexes are higher than its ligand.

Fig. 9. Optimized structures of reactants, transition states (TS), intermediates (IN1) and products
Fig. 10. Bond lengths changes and Mulliken charges changes in the reaction mechanism for 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone molecule.

Fig. 11. Total energy through the IRC for 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone molecule.
The electronic energy data for \textit{I}4\textit{FPTH}_2, calculated with 6-311G(d,p), 6-311++G(d,p), 6-311++G(2d,2p) basis sets in gas phase and DMSO solvent and for Zn[(\textit{I}4\textit{FPTH})\textsubscript{2}], Ni[(\textit{I}4\textit{FPTH})\textsubscript{2}] complexes calculated with 6-31G(d,p), 6-311G(d,p) basis sets are given in Table 1 in au units.

The electronic energy for \textit{I}4\textit{FPTH}_2 calculated with the level of B3LYP/6-31G(d,p), B3LYP/6-311G(d,p), B3LYP/6-311++G(d,p), B3LYP/6-311++G(2d,2p) are -1370.50690942, -1370.75982233, -1370.77771190, -1370.81055509 au, respectively. The lowest electronic energy structure was predicted by B3LYP/6-311++G(2d,2p) in DMSO solvent. Calculated electronic energies in DMSO (-1370.83735522 au) is lower than in gas phase (-1370.81055509 au) for the same basis sets.
Fig. 13. Molecular orbital energies close to HOMO and LUMO for Zn[(I4FPTH)₂] and Ni[(I4FPTH)₂]

Fig. 14. Frontier orbital energies for I4FPTH₂, Zn[(I4FPTH)₂] and Ni[(I4FPTH)₂] calculated with B3LYP/6-311G(d,p) method
3.2 NMR Study

1H and 13C NMR values for I4FPTH2 ligand calculated with 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311++G(2d,2p) basis sets of B3LYP theory in gas phase and DMSO solvent are given in Tables 3 and 4 with the experimental values. 1H and 13C NMR values of Zn[(I4FPTH)2] complex calculated with 6-31G(d,p) and 6-311G(d,p) basis sets with the experimental ones are presented in Table 5.

The correlation coefficient excluding Hydrogen atom belonging to indole ring in 1H NMR calculations performed with B3LYP and 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311++G(2d,2p) basis sets in gas phase is found as 0.856, 0.861, 0.864, 0.888 ppm, respectively and in DMSO solvent 0.773, 0.841, 0.870, 0.870 ppm, respectively (Table 3).

The correlation coefficient of 13C NMR calculations performed with B3LYP and 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311++G(2d,2p) basis sets in gas phase is found as 0.987, 0.984, 0.984, 0.985 ppm, respectively and in DMSO solvent 0.950, 0.941, 0.983, 0.985 ppm, respectively. Correlation coefficients between calculated and observed chemical shifts for 13C NMR carried out with B3LYP and 6-31G(d,p), 6-311G(d,p), 6-311++G(d,p), 6-311++G(2d,2p) basis sets are 0.987, 0.984, 0.984, 0.985 ppm, respectively in DMSO solvent and are in 0.950, 0.941, 0.983, 0.985 ppm in gas phase (Table 4). Accordingly, 1H NMR calculation performed with B3LYP/6-311G(2d,2p) calculation in DMSO gives excellent correlation between computed and observed 13C NMR spectra.

The lack of N-H31 chemical shift belong to thiosemicarbazone group for Zn[(I4FPTH)2] complex which is observed for I4FPTH2 ligand indicates that deprotonation take place during complexation reaction.

3.3 UV Study

UV calculations for molecular structure of I4FPTH2 ligand, Zn[(I4FPTH)2] and Ni[(I4FPTH)2] were simulated by using TDDFT. Oscillator strengths (f) and excitation energies (eV) for UV spectra values of all studied compounds were summarized in Table 6 with the experimental values.

176th molecular orbital calculated with B3LYP/6-31G(d,p) theory is HOMO and 177th molecular orbital is LUMO in the Zn[(I4FPTH)2] complex. The transition observed at 479 nm in the TDB3LYP/6-31G(d,p) level consists of mainly HOMO-1→LUMO and HOMO→LUMO+1 and transition assigned at 266 nm is belong to HOMO-17→LUMO+1, HOMO-16→LUMO, HOMO-2→LUMO+2, HOMO-1→LUMO+2, HOMO→LUMO+3 transitions.
### Table 3. Experimental and theoretical 1H NMR values of 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone molecule

| Atoms | Exp. | 6-31G(d,p) | 6-311G(d,p) | 6-311++G(d,p) | 6-311G(2d,2p) | 6-311G(d,p)-a | 6-311G(d,p)-a | 6-311++G(d,p)-a | 6-311G(2d,2p)-a |
|-------|------|------------|-------------|--------------|---------------|---------------|---------------|----------------|-----------------|
| H29   | 7.74 | 7.66       | 7.79        | 7.75         | 7.93          | 7.92          | 8.05          | 7.91           | 8.20            |
| H24   | 6.92 | 6.72       | 6.85        | 6.82         | 7.00          | 7.25          | 7.41          | 7.19           | 7.55            |
| H32   | 7.13 | 7.14       | 7.22        | 7.18         | 7.38          | 7.43          | 7.58          | 7.41           | 7.73            |
| H25   | 7.35 | 7.34       | 7.43        | 7.40         | 7.62          | 7.74          | 7.87          | 7.71           | 8.06            |
| H28   | 7.58 | 9.89       | 10.00       | 9.97         | 10.32         | 7.94          | 9.85          | 9.66           | 10.17           |
| H23   | 7.58 | 6.72       | 6.89        | 6.85         | 7.11          | 7.60          | 7.45          | 7.33           | 7.66            |
| H27   | 7.27 | 7.07       | 7.23        | 7.19         | 7.39          | 7.49          | 7.64          | 7.53           | 7.81            |
| H22   | 7.27 | 6.97       | 7.10        | 7.06         | 7.29          | 7.51          | 7.64          | 7.53           | 7.82            |
| H30   | 10.83| 9.41       | 9.45        | 9.41         | 10.04         | 9.13          | 9.60          | 9.70           | 10.20           |
| H31   | 11.26| 12.59      | 12.36       | 12.33        | 13.11         | 13.03         | 12.63         | 12.56          | 13.29           |
| H26   | 11.26| 6.22       | 6.25        | 6.21         | 6.77          | 8.17          | 8.24          | 8.36           | 8.76            |
| R²    | 0.856| 0.861      | 0.864       | 0.888        | 0.773         | 0.841         | 0.870         | 0.870          |                 |

### Table 4. Experimental and theoretical 13C NMR values of 3-(N-4-fluorophenyl)-1H-indole-2,3-dione thiosemicarbazone molecule

| Atoms | Exp. | 6-31G(d,p) | 6-311G(d,p) | 6-311++G(d,p) | 6-311G(2d,2p) | 6-311G(d,p)-a | 6-311G(d,p)-a | 6-311++G(d,p)-a | 6-311G(2d,2p)-a |
|-------|------|------------|-------------|--------------|---------------|---------------|---------------|----------------|-----------------|
| C17   | 122  | 116        | 125         | 125          | 125           | 118           | 111           | 128            | 127             |
| C11   | 128  | 118        | 127         | 127          | 128           | 119           | 112           | 131            | 129             |
| C5    | 133  | 125        | 136         | 136          | 136           | 128           | 121           | 140            | 140             |
| C4    | 111  | 105        | 113         | 113          | 114           | 108           | 101           | 118            | 117             |
| C10   | 142  | 136        | 147         | 147          | 148           | 139           | 132           | 151            | 151             |
| C15   | 128  | 117        | 127         | 127          | 128           | 116           | 109           | 127            | 127             |
| C18   | 132  | 123        | 131         | 131          | 131           | 131           | 124           | 139            | 138             |
| C12   | 161  | 154        | 164         | 164          | 167           | 157           | 150           | 171            | 171             |
| C16   | 177  | 169        | 179         | 179          | 181           | 175           | 168           | 184            | 182             |
| C13   | 135  | 129        | 141         | 141          | 142           | 130           | 122           | 144            | 143             |
| C3    | 121  | 115        | 124         | 124          | 124           | 124           | 117           | 129            | 128             |
| C14   | 120  | 115        | 124         | 124          | 125           | 127           | 120           | 125            | 125             |
| C1    | 115  | 111        | 120         | 120          | 120           | 112           | 105           | 124            | 123             |
| C8    | 115  | 112        | 121         | 121          | 121           | 112           | 105           | 122            | 121             |
| C2    | 163  | 155        | 169         | 169          | 169           | 158           | 151           | 171            | 170             |
| R²    | 0.987| 0.984      | 0.984       | 0.985        | 0.950         | 0.941         | 0.983         | 0.985          |                 |

Kandemirli et al.; IRJPAC, 9(1): 1-16, 2015; Article no. IRJPAC.17626
Table 5. Experimental and theoretical 1H NMR and 13C NMR values of Zn[[I4FPTH]2] complex

| Atoms | Exp.  | 6-31G(d,p) | 6-311G(d,p) | Atoms   | Exp.  | 6-31G(d,p) | 6-311G(d,p) |
|-------|-------|------------|-------------|---------|-------|------------|-------------|
| H28   | 6.96  | 6.52       | 6.60        | C17     | 127.8 | 120        | 130         |
| H24   | 7.70  | 7.66       | 7.74        | C31     | 131.3 | 116        | 126         |
| H27   | 7.32  | 6.72       | 6.76        | C5      | 131.5 | 127        | 137         |
| H25   | 7.60  | 7.13       | 7.22        | C4      | 111.7 | 104        | 112         |
| H29   | 6.98  | 6.61       | 6.86        | C10     | 131.7 | 136        | 147         |
| H23   | 7.77  | 10.25      | 10.33       | C15     | 131.3 | 116        | 124         |
| H28   | 7.62  | 7.30       | 7.40        | C18     | 132.1 | 139        | 148         |
| H22   | 7.51  | 6.92       | 7.05        | C12     | 136.3 | 151        | 161         |
| H30   | 10.96 | 6.95       | 7.30        | C16     | 166.6 | 172        | 181         |
| H26   | 10.42 | 6.19       | 6.16        | C13     | 131.6 | 130        | 141         |
|       |       |            |             | C3      | 129.6 | 121        | 130         |
|       |       |            |             | C1      | 122.8 | 113        | 122         |
|       |       |            |             | C8      | 117.2 | 110        | 119         |
|       |       |            |             | C2      | 142.7 | 155        | 169         |

Table 6. Oscillator strengths (f) and excitation energies (eV) for UV spectra values calculated with TDB3LYP and TDB3LYP

| l4FPTH2 | B3LYP | bp86 |
|---------|-------|------|
| Exp(nm) | 6-31G(d,p) | 6-311G(d,p) | 6-311++G(d,p) | 6-311++G(2d,2p) | cep-31g* |
| 371     | 35    | 3.47(0.4) | 35            | 3.47(0.4)       | 36        | 3.42(0.45)E33 | 3.68(0.4) |
| 257     | 256   | 4.85(0.23)| 259           | 4.78(0.23)      | 262       | 4.72(0.19)   | 263         | 4.71(0.18) | 243 | 4.71(0.26) |
|         |       | E10      | E11           |               | E11       | E11          |             |             |         |

| Zn[[l4FPTH]2] | B3LYP |
|---------------|-------|
| Exp(nm) | 6-31G(d,p) | 6-311G(d,p) | 6-311++G(d,p) | 6-311++G(2d,2p) |
| 368     | 47    | 2.59(0.26)E3 | 48            | 2.56(0.30)E3    | 654       | 74          | 1.66(0.08)E3 | 66          | 1.87(0.06)E3 |
| 256     | 266   | 4.66(0.22)E32| 267           | 4.64(0.22)E31   | 436       | 431         | 2.87(0.22)   | 432         | 2.87(0.19)E1 |
|         |       | E31       |               |               | E11       | E11          |             |             |         |
|         |       |           |               |               | 259       | 310          | 3.99(0.10)E3 | 305         | 4.05(0.08)E35 |
|         |       |           |               |               |           | E33          |             |             |         |

Table 7. Experimental and theoretical FTIR spectra of l4FPTH2, Zn[[l4FPTH]2] and Ni[[l4FPTH]2]

| Experimental | u(N6-H26) | u(N19-H30) | v(N20-H31) | v(C=O) | v(C=N) | v(C=S) |
|--------------|-----------|------------|------------|--------|--------|--------|
| l4FPTH2      | 3292      | 3174       | 3073       | 1684   | 1586   | 835    |
| Zn[[l4FPTH]2] | 3381      | 3328       | -          | 1681   | 1575   | 810    |
| Ni[[l4FPTH]2]| 3405      | 3277       | -          | 1660   | 1576   | 812    |

| Theoretical 6-311G(d,p) |
|-------------------------|
| l4FPTH2                | 3643 | 3502 | 3428 | 1776 | 1621 | 958 |
| Zn[[l4FPTH]2]           | 3648 | 3604 | -   | 1793 | 1591 | 820 |
| Ni[[l4FPTH]2]           | 3653 | 3613 | -   | 1791 | 1630 | 833 |
The absorption bands for Zn[(I4FPTH)$_2$] complex observed at 654, 436 and 259 nm were assigned at 744, 431, 310 nm in the calculation with B3LYP/6-31G(d,p) theory, respectively (Table 6).

In the FTIR spectra of I4FPTH$_2$ in above Table 7, the experimental bands at 3292, 3174 and 3073 cm$^{-1}$ correspond to the stretching of $\nu$(N6-H26), $\nu$(N19-H30), and $\nu$(N20–H31) bonds, respectively, whereas $\nu$(N6–H) belong to isatin ring and $\nu$(N19-H30) belong to thiosemicarbazone group were assigned at 3381 and 3328 cm$^{-1}$ for Zn[(I4FPTH)$_2$] and at 3405 and 3277 cm$^{-1}$ for Ni[(I4FPTH)$_2$] complexes, respectively. The $\nu$(N6–H26), $\nu$(N19–H30) and $\nu$(N20–H31) bands stretching of I4FPTH$_2$ compound have been calculated at 3643, 3502 and 3428 cm$^{-1}$ with B3LYP/6-31G(d,p). Whereas in the Zn[(I4FPTH)$_2$] complex, the $\nu$(N6–H) belong to isatin ring and $\nu$(N19–H30) belong to thiosemicarbazone group were assigned at 3648 and 3604 cm$^{-1}$, and assigned at 3653 and 3613 cm$^{-1}$ for Ni[(I4FPTH)$_2$]. The $\nu$(N20–H31) for I4FPTH$_2$ observed at 3073 cm$^{-1}$ was disappeared in Zn[(I4FPTH)$_2$] and Ni[(I4FPTH)$_2$] complexes, it is assumed that this could be due to the dissociation of the proton. The presence of the band at 1681 cm$^{-1}$ in the Zn(II) complex agrees with the uncoordinated nature of the CO group, whereas CO group of I4FPTH$_2$ assigned at 1684 cm$^{-1}$ undergoes a negative shift for Ni[(I4FPTH)$_2$] complex. This indicates coordination also occurs via C=O functional groups in addition to C=N and C=S functional groups.

4. CONCLUSION

Results of quantum chemical calculations of 1H-indole 2,3-dione-3-(N-4-fluorophenyl)thiosemicarbazone and its Zinc (II) and Nickel (II) complexes showed that HOMO energies and polarizibility of complexes are found higher than those ligand. In addition to quantum chemical calculations, experimental values indicates that Zn(II) complex of ligand coordinates via C=N and C=S of its ligand while Ni(II) complex coordinates via C=O C=N and C=S. The results of $^{13}$C NMR calculation with B3LYP/6-311G(2d,2p) method were obtained most sensitive in the all methods.

ACKNOWLEDGEMENTS

Authors thank to Nigde University Scientific Research Projects Unit (NUBAP, Project Number: FEB 2011/01) and Kastamonu University KÜBAP-01/2013-31 for their financial support during this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sriram D, Yogeeswari P, Gopal G. Synthesis, anti-HIV and antitubercular activities of lamivudine prodrugs. European Journal of Medicinal Chemistry. 2005; 40(12):1373–1376.
2. Pandeya SN, Sriram D, Nath G, DeClercq E. Synthesis, antibacterial, antifungal and anti-HIV activities of Schiff and mannich bases derived from isatin derivatives and N-[4-(4-Chlorophenyl)thiazole-2-yl]thiosemicarbazide. European Journal of Pharmaceutical Sciences. 1999;9(1):25–31.
3. Pirrung MC, Pansare SV, Das Sarma K, Keith KA, Kern ER. Combinatorial optimization of isatin-β-thiosemicarbazone as anti-poxvirus agents. Journal of Medicinal Chemistry. 2005;48(8):3045–3050.
4. Bal TR, Anand B, Yogeeswari P, Sriram D. Synthesis and evaluation of anti-HIV activity of isatin β-thiosemicarbazone derivatives. Bioorganic & Medicinal Chemistry Letters. 2005;15(20):4451–4455.
5. Sriram D, Perumal Y. Towards the design and development of agents with broad spectrum chemotherapeutic properties for the effective treatment of HIV/AIDS. Current Medicinal Chemistry. 2003;10(17):1689–1695.
6. Pirrung MC, Pansare SV, Das Sarma K, Keith KA, Kern ER. Combinatorial optimization of isatin-β-thiosemicarbazones as anti-poxvirus agents. Journal of Medicinal Chemistry. 2005;48(8):3045–3050.
7. Bal TR, Anand B, Yogeeswari P, Sriram D. Synthesis and evaluation of anti-HIV activity of isatin β-thiosemicarbazone derivatives. Bioorganic & Medicinal Chemistry Letters. 2005;15(20):4451-4455.
8. Karali N, Terzioglu N, Gurbay A. Synthesis and structure–activity relationships of 3-Hydradono-1H-2-Indolinoses with antituberculosis activity. Arzneimittel Forschung-Drug Research. 1998;48(7):758-763.
9. Sriram D, Yogeeswari P, Gopal G. Synthesis, anti-HIV and antitubercular
activities of lamivudine prodrugs. European Journal of Medicinal Chemistry. 2005; 40(12):1373-1376.

10. Pandeya SN, Sriram D, Nath G, De Clercq E. Synthesis, antibacterial, antifungal and anti-HIV evaluation of schiff and manich bases of isatin and its derivatives with triazole. Arzneimittel Forschung-Drug Research. 2000;50(1):55-59.

11. Kandemirli F, Arslan T, Karadayı N, Köksöy B. Synthesis and theoretical study of 5-Methoxyisatin-3-(N-cyclohexyl)-Thiosemicarbazone and its Ni(II) and Zn(II) complexes. Journal of Molecular Structure. 2009;938(1-3):89-96.

12. Kandemirli F, Arslan T, Köksöy B, Yılmaz M. Synthesis, characterization and theoretical calculations of 5-Methoxyisatin-3-Thiosemicarbazone derivatives. Journal of the Chemical Society of Pakistan. 2009;31(3):498-504.

13. Kandemirli F, Köksöy B, Arslan T, Sagdinc S, Barber H. Synthesis and theoretical study of Bis(fluoroisatinato)mercury(II). Journal of Molecular Structure. 2009;921(1-3):172–177.

14. Gunesoglu Sagdinc S, Kandemirli F, Köksöy B, Bayari SH. Experimental and quantum chemical studies of 5-Fluoroisatin-3-(N-Cyclohexylthiosemicarbazone) and Its metal complexes. Phosphorus, Sulfur, and Silicon, 2012;187(10):1243–1260.

15. Gunesoglu-Sagdinc S, Köksöy B, Kandemirli F, Bayari SH. Theoretical and spectroscopic studies of 5-Fluoro-Isatin-3-(N-Benzylthiosemicarbazone) and its Zinc(II) complex. Journal of Molecular Structure. 2009;917(2):63-70.

16. Karali N, Gürsoy A, Kandemirli F, Shvets N, Kaynak FB, Özsey B, Kovalishyn V, Dimoglo A. Synthesis and structure-antituberculosis activity relationship of 1H-Indole-2,3-Dione derivatives. Bioorganic & Medicinal Chemistry. 2007;15(17):5888-5904.

17. Kandemirli F, Akkaya Y, Vurdu CD. Synthesis and quantum chemical calculations of 4-(2-Fluorophenyl)-1-(2-Oxoidolin-3-ylidene)thiosemicarbazone and Its Zinc(II) complexes. Asian Journal of Chemistry. 2013;25(17):9722-9730.

18. Kandemirli F, Choudhary M I, Siddiq S, Saracoğlu M, Sayiner M, Arslan T, Erbay A, Köksöy B. Quantum chemistry–molecules for innovations. InTech - Open Access Publisher; 2012.

19. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JA, Jr Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam NJ, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas Ő, Foresman JB, Ortiz JV, Cioslowski J, Fox D. Gaussian, Inc, Wallingford CT; 2009.