

Synthesis and characterization of heterocyclic ligand derivatives from 5-amino-2-hydrazino-1,3,4-Thiadiazole and its complex with divalent cadmium

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Abstract— Attempt was carried out to synthesis thiadiazole derivative (2((E)-(2-(5-((E)-2-hydroxybenzylidene) amino)-1,3,4-thiadiazol-2-yl) hydrazono) methyl) phenol) and its complexes with divalent cadmium ion. The ligand and the complex has been characterized by FTIR, ¹HNMR, atomic absorption (AAs) and chlorine detection. Computational modeling using HF-B3LYP/ 3-21G method was performed to identify the coordination modes of the complex to suggest the possible geometry supported by the experimental data.

Index Terms— Thiadiazoles, Schiff base, HOMO – LUMO, heterocyclic.

I. INTRODUCTION

Thiadiazoles are considered within the class of azole compounds containing a *sulfur* and two *nitrogen* atoms which have five membered heterocyclic ring. Thiadiazole derivative compounds have been the focus of attention of researcher in the therapeutic drug field especially for antibacterial treatment^{[1]-[2]}. These compound Possess a good property as ligand toward several metals such as lanthanides and other transition metals to form more potent therapeutic complexes compared with the parent ligand^{[3]-[5]}. The important of the present of thiadiazole ring in these compounds and their complexes may be attributed to:

1-Contribution of nitrogen of the thiadiazole ring in coordination modes through the complexation^{[6]-[9]}.

2-In the absence of chelation through the N atom^{[10]-[12]}, the complex formation is stabilized by π - interaction between CH of phenyl ring and pi electron cloud of thiadiazole ring in the Neighbor unit of the complex^[7].

Computational modeling of quantum chemistry were widely used in the process of ligand metal complexation to investigate some properties of **complex molecules** formed such as their optimized geometries, theoretical vibrational frequencies, bonding in metal complex, free energy, HOMO - LUMO energies and ligand- metal binding mode^{[13]-[17]}.

In this work, attempt were carried out to synthesis thiadiazole derivative and its complex with cadmium and to determine the binding modes of the complex through computational modeling to suggest the final geometry of the complex.

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II. EXPERIMENTAL

All chemicals used for the synthesis and measurements were high purity products, while the purity of the compounds was checked on the thin layer chromatography (TLC) plates (Silica gel G). FTIR, ¹HNMR, atomic absorption and the usual method for the determination of chlorine ion were used to characterize the complex, The FTIR spectra was obtained on a FT-IR spectrometer (PERKIN ELMER SPEACTUM-65) in Diyala University. The ¹H-NMR spectra (solvent DMSO-d₆) was obtained on Bruker 60 MHz spectrophotometer using TMS as internal standard. The melting points of the synthesized compounds were determined by capillary melting point apparatus.

Synthetic methods

Synthesis of 5-amino-2-hydrazino-1,3,4-thiadiazole

This compound was Prepared from 5-amino-2-mercapto-1,3,4-thiadiazole and hydrazine according to Nadia Adil method^[18] as dark white crystals. Yield (78 %), m.p 218-220°C, FT- IR data in (cm⁻¹): 3250-3397 ν (NHNH₂), 3197 ν (NH₂), 1583 ν (C=N), 1022 ν (N-N), 685 ν (C-S).

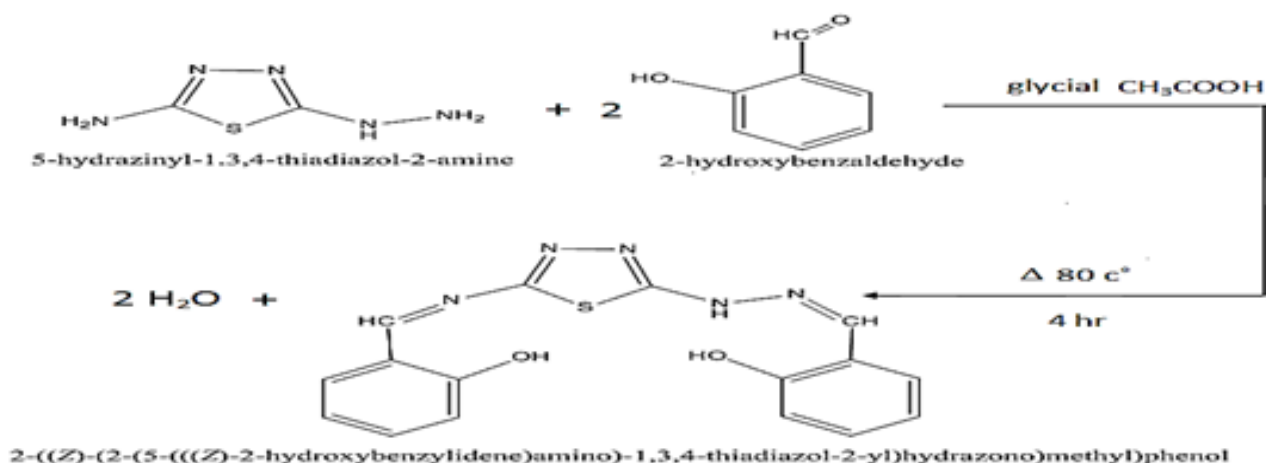
Synthesis of Ligand

O-hydroxy benzaldehyde (0.01mol, 1.221 gm) was dissolved in 25 ml distilled ethanol and added to (0.005mol,0.658 gm) of 5-amino-2-hydrazino-1,3,4-thiadiazole which dissolved in 50 ml distilled ethanol. Then, 4-5 drops of glacial acetic acid was added into the mixture. The mixture was refluxed in a water bath at 80°C, the progress of the reaction was monitored by TLC. After 4 hours, the reaction was completed as indicated by TLC. The mixture was left stirring overnight at room temperature. Golden yellow precipitate was formed in the next day, flitted off, washed with cold ethanol and dried. Yield (60 %), m.p 247-249°C, FT- IR data in (cm⁻¹): 3178 ν (N-H), 1619 ν (CH=N), 1604 ν (CH=N), 1567 ν (C=C), 1237 ν (C-N) and 1267 ν (C-O), 676 ν (C-S). ¹H-NMR (DMSO-d₆) δ : 11.40 (s, H, NH), 10.49 and 10.10(s, 2H, OH phenolic), 9.10 and 8.68 (s, 2H, CH=N), 7.86- 6.89 (m,8Ar-H).

Synthesis of complex

To a solution of (0.678 gm, 0.002 mol) from the ligand in 30 ml absolute ethanol, a solution of (0.438 gm, 0.002 mol) CdCl₂.2H₂O in 30 ml absolute ethanol was added gradually at pH= 8.5 by adding **many drops** of 5 % KOH. The mixture was refluxed with constant stirring for 2 hours at 78 C^o. Orange precipitate was formed after cooling and followed by washing with ethanol several times.

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III. RESULTS AND DISCUSSION

FTIR study

As shown in fig- 1&2 , in free ligand, broadband in the region of (3300-2600 cm⁻¹) assigned to hydrogen bonded OH was recorded and the disappearance of this band upon complexation indicates its coordination to cadmium ion due to the deprotonation of hydroxyl groups. The spectrum of the

ligand shows strong band at (3178 cm⁻¹) which is attributed to N-H attached to thiadiazole ring, this band remain as it is after complex formation.(3179 cm⁻¹) which excludes the involvement of nitrogen amine in the coordination. Two strong C=N stretching bands appear at 1619 and 1604cm⁻¹, these bands were shifted to lower frequency upon complexation which provide evidence that these are contributed in the coordination.

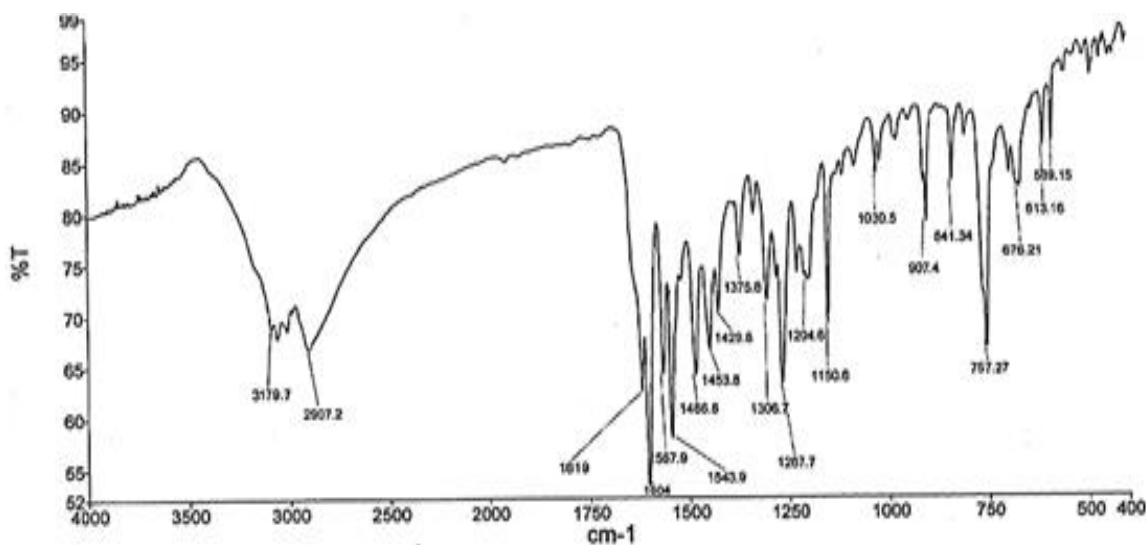


Fig-1: FT-IR spectra of the ligand

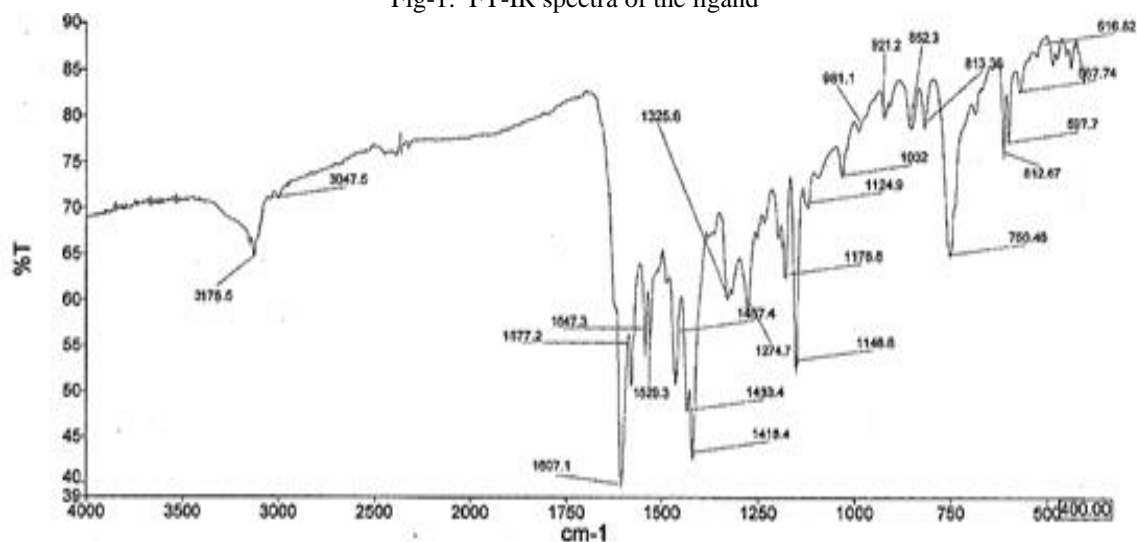


Fig-2: : FT-IR spectra of the complex

¹H-NMR Spectra:

As obtained in fig-3&4, the ¹H-NMR spectra of the ligand show a signal at $\delta(11.4 \text{ ppm})$ which refers to the proton of (NH) attached with thiadiazole^[19], also two peaks appeared at $\delta(10.10 \text{ and } 10.49 \text{ ppm})$ which attributed to the protons of the two different sites of hydroxyl groups^[20]. And the two peaks appeared at $\delta(8.68 \text{ and } 9.10 \text{ ppm})$ are attributed to the protons of of **azomethine hydrogens** (HC=N). The multiple peaks appeared between $\delta(6.89 - 7.86 \text{ ppm})$ refer to 8 protons of two aromatic rings^[21]. In ¹H-NMR of

complex, the signals of (NH) appeared at the same position in the ligand spectrum and that reflects no participation of this nitrogen in metal coordination. **disappearance of hydroxyl proton** signals is clear evidence of the involvement of **deprotonated hydroxyl** groups in the coordination with cadmium ion. The shifting of **azomethine hydrogens** (-N=CH-) from $\delta(8.68 \text{ and } 9.10 \text{ ppm})$ on ligand spectrum to $\delta(8.35 \text{ and } 8.78 \text{ ppm})$ on cadmium complex respectively is supportive of the chelation of azomethine nitrogen to cadmium ion.

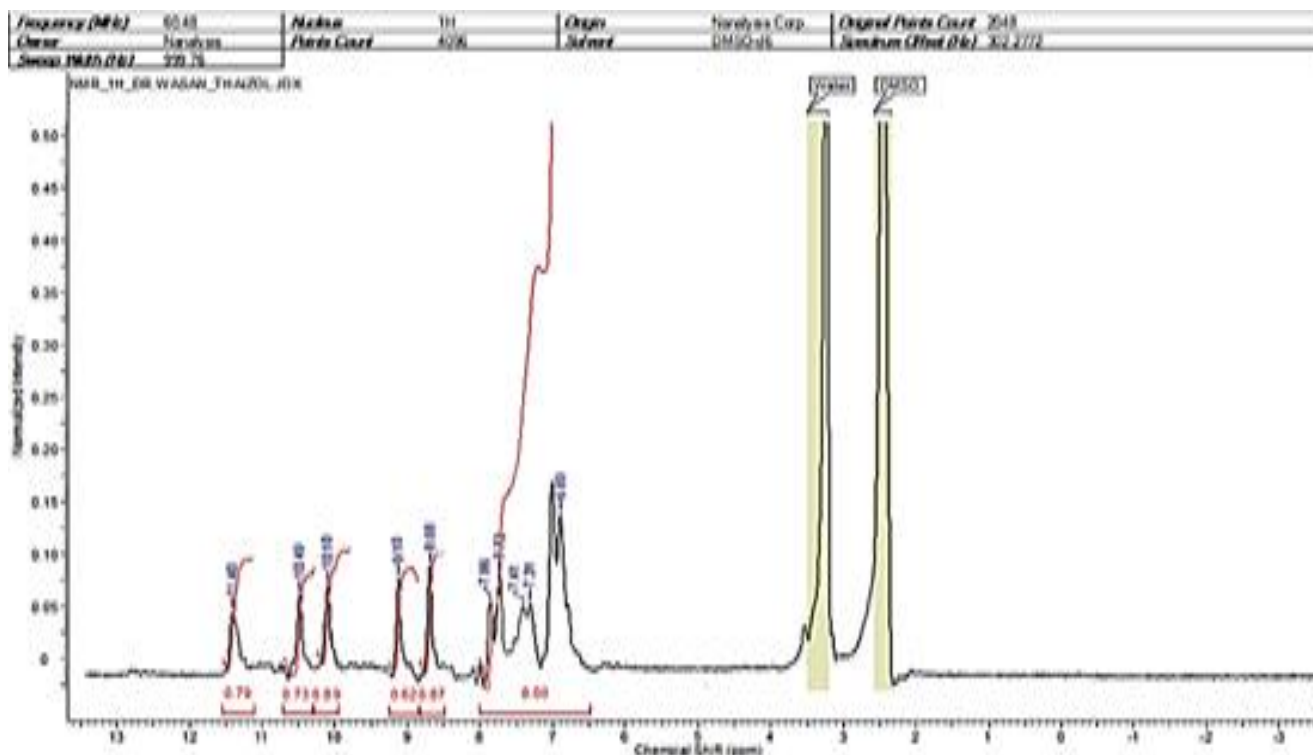
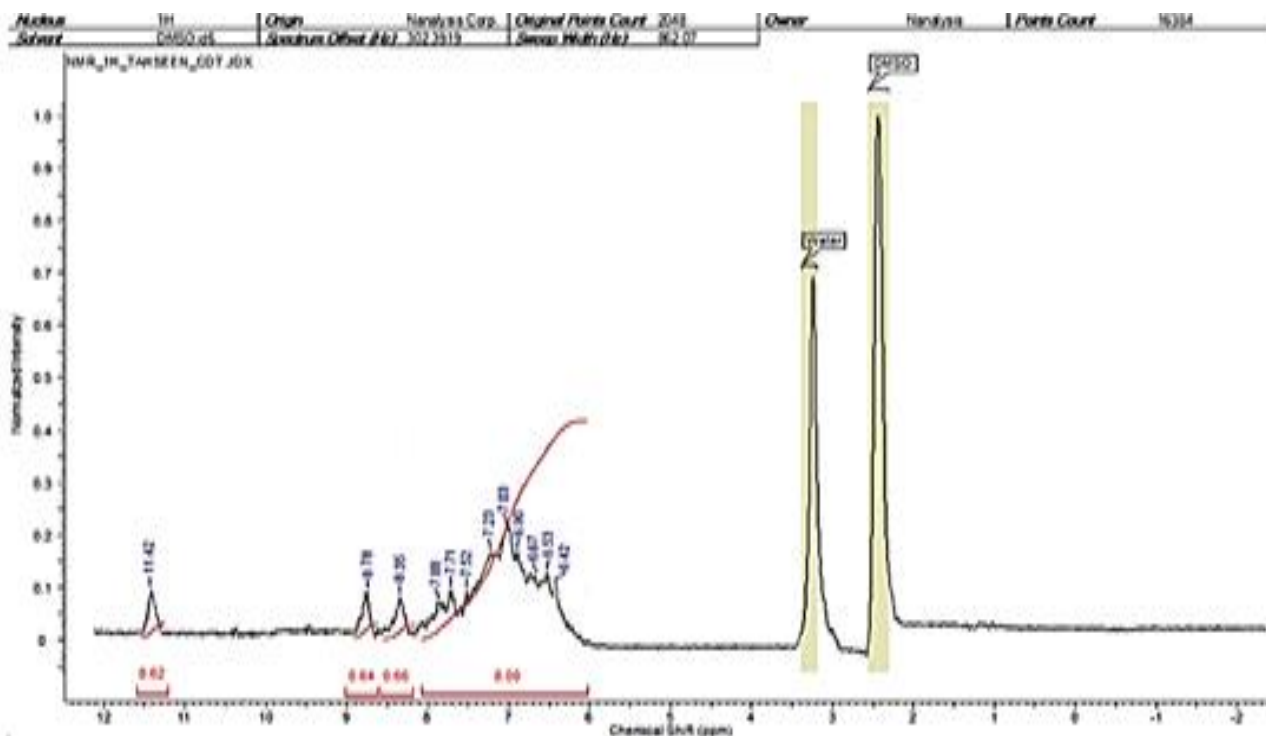


Fig-3: ¹H-NMR Spectra of the ligand



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Computational approach

A number of chelation possibilities were considered to investigate the complex geometry according to HOMO-LUMO energy gap (E_{gap}) which revealed that "the more E_{gap} means the more stability of complex" [22],[23]. Bidentate mode binding, case no. 1-5 shown in table-1 reflect that the deprotonated hydroxyl group (case no.1) is the best probability among the fifth studied cases due to its higher value of E_{gap} . Starting from this point, the rest possibilities have been studied. It can be concluded that:

1- It must exclude any presence of chlorine in the complex (case no. 6,7,18,20,26).

which supported by chlorine analysis

2- Non octahedral geometry are expected (case no 26 and 27).

3- All the following atoms (N2, N3, N6, S5) are non involved in the coordination sphere.

4- **Azomethine nitrogens** (N7 and N16) are contributed in the chelation mode of the complex

5- It can be considered that the tetrahedral geometry is the most suggested one but this probability is distributed equally among tetradentate behavior of the ligand (case no. 22) and tridentate chelator of the ligand plus water molecule in the coordination sphere case.no.21). This geometry is supported by atomic absorption measurement of cadmium metal content which is found 23.57% (calculated 24.9%) and the mole ratio of metal/ligand (1:1). Figures 5-7 show the ligand and the suggested geometries

Table-1: Chelation modes possibilities of cadmium complex optimized by HF-B3LYP/ 3-21G

Bidentate chelating mode		
Case No.	Chelation sites	gap (ev)
1	Cd + O24 + O15)	(3.906
2	Cd + N7 + N16)	(0.468
3	Cd + N6 + N16)	(X*
4	Cd + N7 + O24)	(X
5	Cd + N16 + O15)	(X
6	Cd + O24 + O15) + 2Cl	(X
7	Cd + N7 + N16) + 2Cl	(X
8	Cd + O24 + O15) + 2H ₂ O	(3.977
9	Cd + N7 + N16) + 2H ₂ O	(X
Tridentate chelating mode		
10	Cd + N7 + N16 + O15)	(0.448
11	Cd + N6 + N16 + O24)	(X
12	Cd + N7 + O24 + O15)	(3.422
13	Cd + N16 + O24 + O15)	(4.445
14	Cd+N6 + O24 + O15)	(X
15	Cd + N7 + N16+O24)	(X
16	Cd + N6 + N16+O24)	(X
17	Cd + N6 + N16+O15)	(X
18	Cd+N16 + O24 + O15) + Cl	(X
19	Cd+N16 + O24 + O15) + H ₂ O	(X
20	Cd + N7 + O24 + O15) + Cl	(X
21	Cd + N7 + O24 + O15) + H ₂ O	(4.963
Tetradentate chelating mode		
22	Cd + N7 + N1 + O24 + O15)	(4.636
23	Cd + N7 + N16 + ^H O24 + ^H O15)	(0.708
24	Cd + N7 + N16 + O24 + ^H O15)	(0.399
25	Cd + N7 + N16 + ^H O24 + O15)	(0.236
26	Cd + N7 + N16 + O24+ O15) + 2Cl	(X
27	Cd + N7 + N16 + O24 + O15) + 2H ₂ O	(X

X* distorted bond or bonds

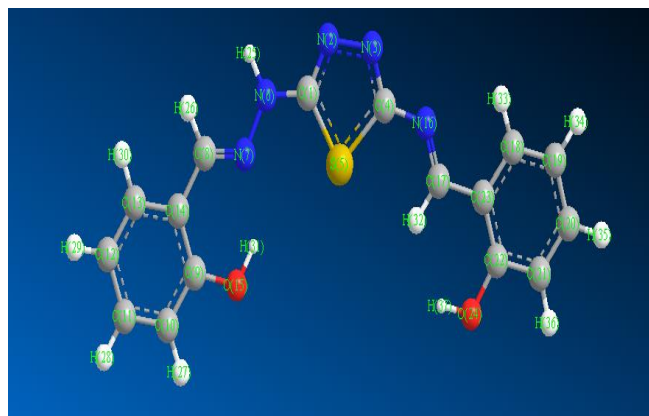


Fig-5: Optimized structure of ligand calculated by HF-B3LYP/ 3-21G

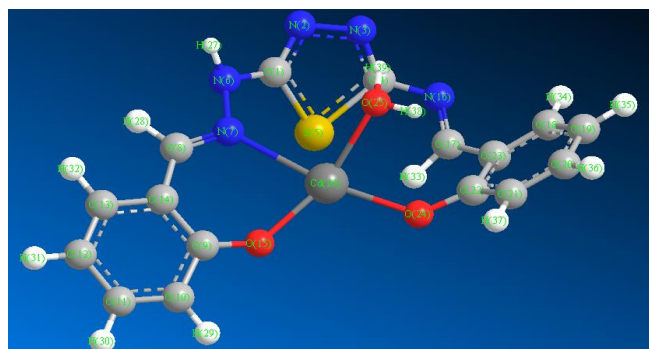


Fig-6: Optimized structure of cadmium complex (case no.21) calculated by HF-B3LYP/ 3-21G

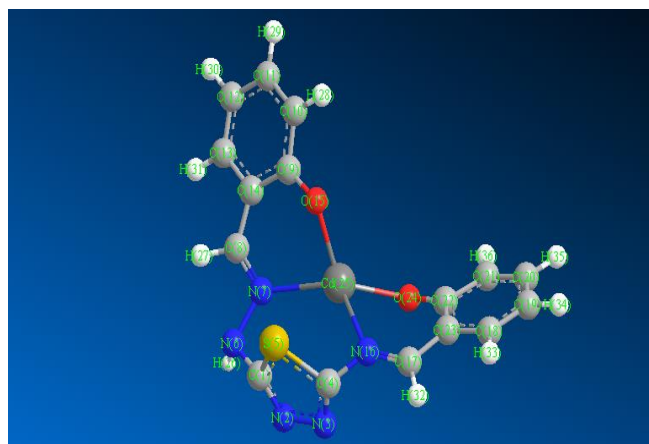


Fig-7: Optimized structure of cadmium complex (case no.22) calculated by HF-B3LYP/ 3-21G

IV. CONCLUSION

The ligand of (2((E)-(2-(5-(((E)-2-hydroxybenzylidene)amino)-1,3,4-thiazol-2-yl)hydrazono)methyl)phenol) and its cadmium divalent complex were synthesized and characterization by FTIR, ¹HNMR, AAs spectroscopies and chlorine analysis. The geometry of ligand and its metal complex were optimized by Computational modeling using HF-B3LYP/ 3-21G method as well as the HOMO, LUMO and E_{GAP} were determined by this method. The Computational and Experimental results showed that the ligand acted as either tetradentate from N,N,O,O' or tridentate plus water molecule.

REFERENCES

- [1] Gupta Y., Agarwal S., Madnawat S. and Ram N., Synthesis and Antimicrobial Activities of Mn (II) and Fe (III) Complexes with N-S donor Ligand, *Research Journal of Chemistry and Environment*, (2012),16(2): 48-51.
- [2] Adedij J., Adebayo M., Ajayi Y. and Yusuf L., Novel mixed ligand of 2,5-diamino-1,3,4-thiadiazole schiff base incorporating benzoic acid: Synthesis and antimicrobial activity, *Journal of Chemical and Pharmaceutical Research*, 2012, 4(3):1501-1504
- [3] Nasser D., Synthesis and Characterization of Complexes of Some Lanthanide Metals With 2-amino-5-(4-hexyloxyphenyl)-1,3,4-thiadiazole., *Proceeding of 3rd scientific conference of the College of Science, University of Baghdad*, (2009),1482-1487.
- [4] Ahemd A., Reyahd A. and Ismaeel M., Synthesis and Characterization of New Schiff Bases and Using Them Us Tri Dentate Ligands in Metal Complexes, *International Journal of Applied Science and Technology*,(2014) 4(6):108-112.
- [5] Suman M., Suparna G. and Liviu M., Complexes of some 3d-metals with a Schiff base derived from 5-acetamido-1,3,4-thiadiazole-2-sulphonamide and their biological activity, *J. Serb. Chem. Soc.*(2011), 76 (10) 1387–1394.
- [6] Gehad G., Zayed M. and Abdallah S., Metal complexes of a novel Schiff base derived from sulphametrole and varelaldehyde. Synthesis, spectral, thermal characterization and biological activity, *Journal of Molecular Structure* (2010), 979 62–71.
- [7] Bharti A., Bharati P., Ram D., Bharty M., Dheeraj K. and Singh N., Studies on phenylmercury(II) complexes of nitrogen–sulfur ligands: Synthesis, spectral, structural characterization, TD-DFT and photoluminescent properties, *Polyhedron* (2013), 65:170–180
- [8] Abdalla M. and Hadi M., Synthesis, Spectral, Thermal Analyses and Molecular Modeling of Bioactive Cu(II)-complexes with 1,3,4-thiadiazole Schiff Base Derivatives. Their Catalytic Effect on the Cathodic Reduction of Oxygen, *Int. J. Electrochem. Sci.*, (2012), 7: 10074 - 10093
- [9] Srivastava K., Ashwini K. and Rakesh S., Bivalent transition metal complexes of tridentate schiff base ligands: An ecofriendly Study, *J. Chem. Pharm. Res.*, 2010, 2(6):68-77.
- [10] Johnson F., Matthew A., Oluwatosin B., Yetunde C. and Omokehinde F., Synthesis and Antitubercular Activities of Cu(II) Metal Complexes with some Semicarbazide Derivatives., *The Pacific Journal of Science and Technology*, 2013, 14(1):251-258.
- [11] Yip F., EmadY., Sie T. and Ahmed M., Synthesis, Characterization and Preliminary *in vitro* Antibacterial Screening Activity of Metal Complexes Derivatives of 2-{{[5-(4-Nitrophenyl)-1,3,4-thiadiazol-2-ylimino]methyl}phenol}, *Asian Journal of Chemistry*;2013,25(8):4203-4206.
- [12] Laurence B., Karl K. and Dieter T., Mn Manganese: Coordination Compounds ,*Gmelin Handbook of inorganic chemistry*, 8th ed., Springer Verlag Berlin Heidelberg, London, 1990.
- [13] Beyramabadi.S., DFT Study on the Fe, Cu and Zn Complexes of 4-(2-Thiazolylazo) Resorcinol, *Bulgarian Chemical Communications*, 2014, 46(1:) 31 – 35.
- [14] Charity F., Gernot F. and Gregory S., Donor–Acceptor Properties of Bidentate Phosphines. DFT Study of Nickel Carbonyls and Molecular Dihydrogen Complexes, *Organometallics*, 2012, 31: 4122–4132
- [15] Rodrigo C., Joaquin O., Josefa D., Juan F. and Francisco M., Theoretical calculations of stability constants and pKa values of metal complexes in solution: application to pyridoxamine–copper(II) complexes and their biological implications in AGE inhibition, *Phys.Chem. Chem. Phys.*, 2013, 15:16303-16312.
- [16] Singh R., Suresh K., and Prabhu D., Frontier Orbitals of Transition Metal Halides and Thioamides *International Journal of ChemTech Research*, 2011, 3(3):1571-1579.
- [17] Mihaylov T., Trendafilova N., Kostova I., Georgieva I. and Bauer G., DFT modeling and spectroscopic study of metal–ligand bonding in La(III) complex of coumarin-3-carboxylic acid, *Chemical Physics*, (2006), 327, 209–219.
- [18] Nadia A., Synthesis and Characterization of Novel Azole Heterocycles Based on 2,5-Disubstituted Thiadiazole, *Turk J. Chem.* (2008) , 32, 229 – 235.
- [19] Faraj F., Khaledi H., Morimoto Y., Itoh S., Olmstead M. M. and Ali H. M., Atetradentate β -Diimino Ligand containing phenolate substituents: Flexivalent coordination to Mn^{III}, Co^{III},Ni^{II},Cu^{II}, *Eur. J. Inorg. Chem.*, 2014, 10(33), p 5752-5759.
- [20] Ahmed A. and Majed R., Synthesis and characterization of new Schiff bases and using them us tridentate ligands in metal complexes, *Inter. J.of app. Scie. and tech.*, 2014 , 4(6), 108-112.
- [21] Faraj F., Metal Coordination Behaviour And Biological activities of Indole and Quinazoline Derivatives, Ph.D. Thesis, University Of Malaya, Kuala Lumpur, Malaysia, 2015.
- [22] Li S.F., Xinlian X., Hao Z., Xinchuang N., Fei W., Sun Q., Yu J., Guo Z. and Shevlin S., High inertness of W@Si12 cluster toward O2 molecule, *Physics Letters A*, (2012), 376:1454–1459.
- [23] Salihovi M., Huseinović Š., Špirtović H., Osmanović S., Dedić A.c ,Ašimović A., Završnik D., DFT Study and Biological Activity of Some Methylxanthines, *Bull. of Chem. and Tech.of Bosn. and Herz.*, 2014, 42:31-36