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Hartree-Fock, molecular docking, spectral, kinetic and antitumor considerations for cobalt, nickel, palladium and platinum (II)-bis carbothiohydrazide complexes

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ABSTRACT

New metal ion complexes were synthesized using Schiff base derivative and characterized using spectral and theoretical analysis. IR and 1H NMR spectra, suggest bi-dentate to tetra-dentate mode of bonding each towards two metal ions. Square-planar and octahedral configurations are the two proposed geometries for Pd(II) or Pt(II) and Co(II) or Ni(II) complexes, respectively. Significant spectral parameters were calculated to emphasis on the type of bonds between active sites and the metal atoms. XRD patterns and TEM images stressed on the nanometer sized appearance for all investigated compounds. Theoretical considerations were implemented using Gaussian09 and Autodock computational tools. HF/LANL2DZ molecular modeling exerts the optimized structures which agree with the spectral data. The frontier molecular orbitals, HOMO and LUMO were calculated. Also, the calculated geometric parameters foresee the distinguish bioactive features of all compounds under interest. Molecular docking utilizes defiant protein receptors attributed to the microorganisms executed in biological application as; 3t88, 3ty7, 3cku, 2ylh and 2jrs. Considerable reduction in binding energies was recorded along the docking process. The docked Schiff base ligand displays significant energy data with *hepatocellular carcinoma* (2jrs) and *Escherichia coli* (3t88) receptors. This deducts the affinity of designed drug against the two infections. The antibacterial and antifungal activities were tested against different microorganisms. The scanned compounds display a comparable inhibition activity along the investigation process. IC_{50} was determined for all compounds against hepatocellular carcinoma cells. Co(II) and Ni(II) complexes are introducing an excellent activity towards the inhibition of all microorganisms and also offer the best IC_{50} values in carcinoma cell line investigation.

1. Introduction

In the last few decades the Schiff base ligands include NSO donors have attracted the researcher insight to intensify the research dealing with such chelating compounds. Schiff base metal ion complexes are taken a great attention due to their enormous application in different areas based on the role of metal ion in enhancement the activity at all. Antitumor, antiaprotozoal and antibacterial activates are recorded with different thiosemicarbazone complexes [1–4]. A series of salicylaldehyde thiosemicarbazone complexes have been synthesized using Pd(II), Cu(II) and Ru(III) ions. The complexes isolated have 1:1 and 1:2 (M:L) molar ratios [5]. Also, vanadium complex was prepared from salicylaldehyde thiosemicarbazone and tri-dentate mode of bonding was proposed through ONS donors [6]. Generally, the divalent metal ion complexes have been used for the complexation towards diprotic Schiff base ligands with N_2O_2 donors [7,8]. In continuation for previous work [9–15], here in our study we are dealing with bis derivative for thiocarbohdrazide with salicylaldehyde. The bis derivative includes multi-donor centers which enriches the coordination towards bivalent cobalt and nickel group metals. The spectral, thermal and kinetic studies will be used to establish the structural formula of the complexes. Gaussian09 molecular modeling and Autodock molecular docking will be elaborately implemented to serve the chemical and biological investigations.

2. Experimental

2.1. Reagents

The chemicals concerned in this study to prepare the Schiff base ligand are, thiocarbohydrazide and salicyladehyde were purchased from Fulka and employed as it is. Also, the metal chloride salts used for complexation as; $CoCl_2(H_2O)_6$, $NiCl_2(H_2O)_6$, $PdCl_2$ and, $PtCl_2$ are commercially available from Sigma-Aldrich. The solvents used in synthesis process are utilized without previous purification.

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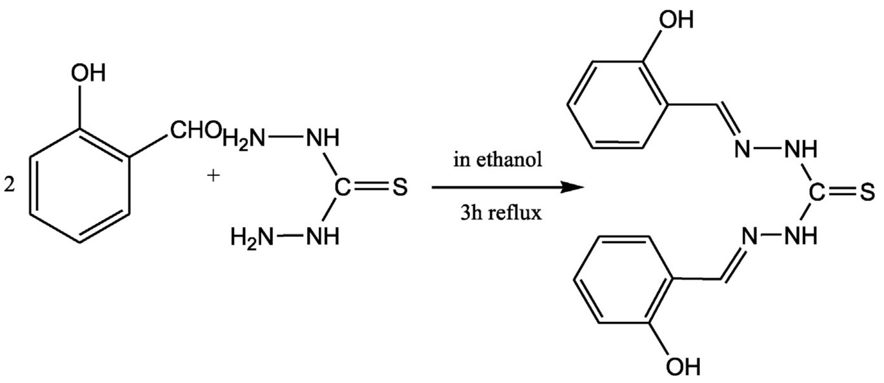


Scheme 1. Synthesis of *N*′,2-bis((*E*)-2-hydroxybenzylidene) hydrazine-1-carbothiohydrazide.

2.2. Synthesis

2.2.1. Synthesis of N′,2-bis((E)-2-hydroxybenzylidene) hydrazine-1-carbothiohydrazide (H_3L)

In a round bottom flask, 1:2 M ratio from thiocarbohydrazide (5 mmol, 0.50 g) to salicyldehyde (10 mmol, 1.722 g) is condensed in ethanolic solution (40 mL) (Scheme 1). The mixture was refluxed for ≈3 h, allowed to cool down. The yellow precipitate Schiff base product was collected by filtration, washed with ether and re-crystallized in ethanol by a suitable yield (65%). The elemental analyses are; C; 57.36 (calcd. 57.30%), H; 4.48(calcd. 4.49%) and N; 18.83 (calcd. 17.82%). The structural formula of the ligand ($C_{15}H_{14}N_4O_2S$) was verified by spectral analysis.

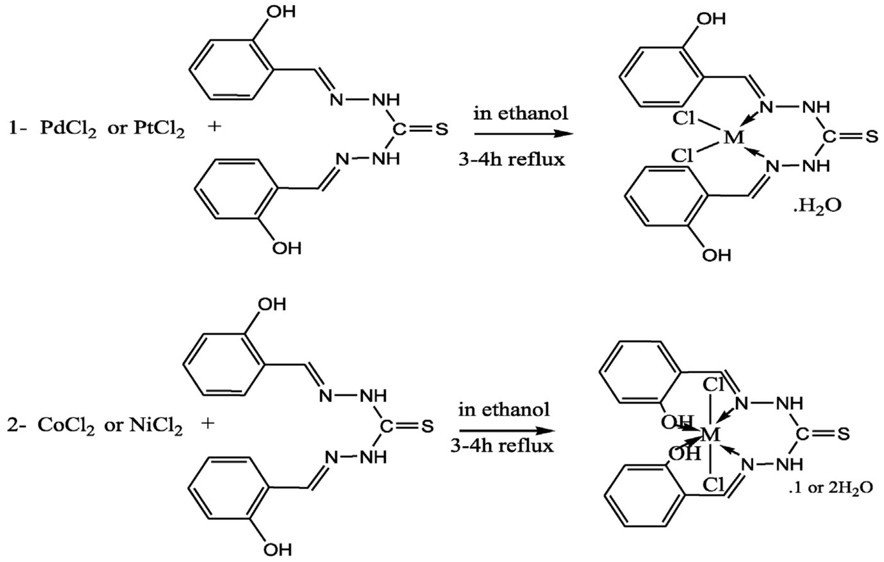
2.2.2. Synthesis of metal ion complexes

The synthesis process were carried out (Scheme 2) at the same conditions except the Co(II) complex. The precipitation of Co(II) complex needs few drops of tri-ethylamine to accelerate the reaction which sometimes distinguish cobalt complexation. Equi-molar ratios (1:1) were mixed from Schiff base ligand to each metal salt. 0.3144 g (1 mmol) of ligand dissolved in ethanol, was added drop wisely to metal chloride solution attributed to, $CoCl_2(H_2O)_6$(0.238 g); $NiCl_2(H_2O)_6$(0.238 g); $PdCl_2$(0.177 g) and $PtCl_2$(0.266 g). The mixtures refluxed for 3–4 h, the precipitates were filtered off washed with ethanol, diethyl ether and finally dried in a vacuum desiccator.

2.3. Biological activity

2.3.1. Anti-microorganisms activity

The compounds under investigation were tested individually against bacteria, *Escherichia coli* (G−) and *Staphlococcus aureus (G+)* and fungi as; *Aspergillus fumigatus and canadida albicans*. The biological investigation was implemented using agar well diffusion methods



Scheme 2. The synthesis process of complexes.

Table 1
Analytical and physical data of H_3L Schiff base ligand and its metal complexes.

Compound empirical formula (Calcd)	Color	Elemental analysis (%) Calcd/Found				
		C	H	N	M	Cl
1) [$C_{15}H_{14}N_4O_2S$] (314.35)	Yellow	57.30/57.36	4.49/4.48	17.82/17.83	–	
2) [$Co(Cl)_2(C_{15}H_{14}N_4O_2S)$]($H_2O$)(462.21)	Brown	38.98/38.99	3.49/3.52	12.12/12.14	12.75/12.80	15.34/15.44
3) [$Ni(Cl)_2(C_{15}H_{14}N_4O_2S)$]($H_2O)_2$(479.97)	Dark green	37.54/37.8	3.78/3.77	11.67/11.64	12.23/12.22	14.77/14.55
4) [$Pd(Cl)_2(C_{15}H_{14}N_4O_2S)$]($H_2O$)(509.69)	Orange	35.35/35.40	3.16/3.20	10.99/11.10	20.88/20.87	13.91/13.92
5) [$Pt(Cl)_2(C_{15}H_{14}N_4O_2S)$]($H_2O$)(598.34)	Brownish yellow	30.11/30.13	2.69/2.67	9.36/9.40	32.60/32.61	11.85/11.88