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2-(2-(2-Hydroxybenzyliden) Hydrazinyl)-2- Oxo-N-(Pyridine-2-Yl)Acetamide Complexes: Synthesis, Characterization And Biological Studies .

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1 - ABSTRACT

2-(2-(2-hydroxybenzyliden) hydrazinyl)-2-oxo-N-(pyridine-2-yl) acetamide complexes of Ni(II) and Co(II) prepared. The proposed structures proved based on elemental, DFT, and spectral analysis. The DNA binding affinity and MIC activity against Gram-positive, Gram-negative bacteria, pathogenic C. albicans and A. flavus fungal strain tested.

Keywords: Hydrazones, DFT, DND, Potentiometry

(4000–400 cm-1) in KBr discs. While; the electronic spectra of complexes (in DMSO solution) was recorded using a Perkin Elmer Lamda 25 UV/Vis Spectrophotometer.1H , 13C-NMR measurements were done on Mercury and Gemini 400 MHZ spectrometer at room temperature in d6-DMSO. pH–meter HANNA -8519, Italy used in all pH- metric measurements.

2.2. Synthesis

2.2.1 Preparation of ligand (H2L)

i. Preparation of ethyl 2-oxo-2-(pyridin-2-ylamino)acetate:

ethyl 2-oxo-2-(pyridin-2-ylamino)acetate were prepared by adding of diethyl oxalate (1 mmol) dissolved in xylene to 2-amino pyridine (1 mmol) dissolved in xylene with stirring followed by reflux with

2 .Experimental

2.1.Instrumentation

(C, H and N) percent presented in the prepared ligand (H2L) and complexes were detected using a Perkin–Elmer 2400 series II analyzer, while chloride and metal contents determined using standard methods reported previously [15]. A thermogravimetric analyzer (TGA-50H) from Shimadzu, Japan, used for both thermogravimetric (TGA) and differential thermal analysis (DTA) measurements with a heating rate of 10 oC/min on at temperature range (20–800oC) and nitrogen flow rate of 15 ml/min. A Sherwood Magnetic Balance was utilized to measure the magnetic susceptibility of solid complexes. A Mattson 5000 FTIR spectrophotometer was used to analyze the prepared ligand and complexes under range of

All the complexes were prepared by refluxing 1 mmol of ligand under investigation with 1 mmol of the metal salt, NiCl2.6H2O, and CoCl2.6H2O in an ethanolic solution on a water bath for 2 – 3 h. The resulting solid complexes filtered off, washed several times with absolute ethanol and finally dried.

2.3. Molecular modeling

Cluster calculations were evaluated using DMOL3 program [16] in Materials Studio package [17]. This program designed for the calculations of density functional theory (DFT) over a large scale. Moreover, DFT method was applied to calculate the semi-core pseudopods (dspp) by using the double numerical basis sets plus polarization functional (DNP). Delley et al. revealed that the DNP basis sets are more precise than Gaussian basis sets of the same size [18, 19]. Lately; the RPBE basis sets are the best exchange–correlation functional [20, 21]. It utilized for the determination of both the exchange and correlation effects of electrons based on the generalized gradient approximation (GGA). The geometric design predicted without any symmetry restriction.

2.4. pH-metric study

Potentiometric titrations were done at 298, 308 and 318◦K in a mixture of dioxane-water 50% (v/v). All resulted values were adjusted using Van Uitert and Hass relation [22]:

Where and are the correction factors for the solvent composition and ionic

stirring for 3 hr. Let the resulted product to cool then filtered off, washed by ether and at the end dried over anhydrous calcium chloride in a vacuum desiccator. The product is yellow color powder with m. p (180 oC)

ii. Preparation of 2-hydrazinyl-2-oxo-N-(pyridin-2-yl)acetamide:

2-hydrazinyl-2-oxo-N-(pyridin-2-yl)acetamide were prepared by adding of hydrazine hydrate (1 mmol) dissolved in xylene to ethyl 2-oxo-2-(pyridin-2-ylamino)acetate (1 mmol) dissolved in xylene with stirring followed by reflux with stirring for 3 hr. Let the resulted product to cool then filtered off, washed by ether and at the end dried in a vacuum desiccator over anhydrous calcium chloride. The resulted ligand is a yellow color powder with m. p (195 oC)

iii. Preparation of ligand (H2L)

1:1 molar ratio of 2-hydrazinyl-2-oxo-N-(pyridin-2-yl) acetamide and 2-hydroxybenzaldehyde (salicylaldehyde) were mixed in a hot ethanolic solution with few drops of glacial acetic acid. The mixture was refluxed for 4 h under magnetic stirring. The formed products was separated by filtration, and then recrystallized from ethanol absolute. Finally, the resulted ligand was dried for 36 h in a vacuum desiccator, then investigated by TLC, elemental analysis (C, H and N), and spectroscopic methods (IR, UV-Vis., 1H NMR, 13C NMR and EI-mass).

2.2.2. Preparation of solid complexes

subtilis are examples for gram positive bacteria and *Escherichia coli*, *Pseudomonas aeuroginosa* are gram negative bacetria. All samples were tested in a Muller Hinton agar medium (Oxoid). Also; the anti-fungal activity for these compounds against *(Candidaalbicans*and*Aspergillusflavus)* was checked in Sabouraud dextrose agar medium (Oxoid). Ampicillin as anti-bacterial and Colitrimazole Fluconazole as anti-fungal were used as standard materials.

MIC [23] of the respective compounds were measured by agar streak dilution method. All steps of the experiments were carried out as reported previously [24]

2.5.2. Colorimetric assay for compounds that bind DNA [25]

A suspended solution of 20 mg of DNA methyl green was prepared in 100 ml of Tris-HCl (0.05 M), buffered at pH 7.5 and contains 7.5 mM MgSO4. This mixture was stirred for 24 h at 37 °C. In an ependoff tubes, 10, 100, 1000 mg of test samples dissolved in ethanol were prepared, then solvent was removed under vacuum, and 200µl of the DNA/methyl green solution were added to all tubes. All samples were incubated for 24 h in the dark at ambient temperature, and then the absorbance values for the samples were evaluated at 642.5-645 nm. Reading values were corrected according to the initial absorbance of the untreated standard.

REFERENCES:-

strength, respectively and B is the reading.

In the experiments; the following mixtures were titrated against standardized free carbonate NaOH solution ($8.5x10^{-3}$,mol L^{-1}) in 50% (v/v) DMSO-water at constant ionic strength (1mol L^{-1}KCl solution) The solution mixtures (i-iii) were prepared as follows:

i) 1.25 ml HCl ($1.12 x10^{-2}$ M) + 1.25 ml KCl (1 M) + 12.5 ml DMSO +10 ml bidistilled H_2O.

ii) 1.25 ml HCl ($1.12x10^{-2}$ M) + 1.25 ml KCl (1M) + 2.5 ml($5x10^{-3}$ M) H_2PET + 10 ml DMSO + 10 ml bidistilled H_2O.

iii) 1.25 ml HCl ($1.12x10^{-2}$ M) + 1.25 ml KCl (1M) + 2.5 ml ($5x10^{-3}$ M) H_2PET + 10 ml DMSO + 0.5 ml metal ion (M^{n+}) ($5x10^{-3}$ M) , [where M^{n+}=Co(II)] + 9.5 ml bidistilled H_2O.

The total volume attuned to 25 ml by DMSO in each prepared mixture .

2.5. Biological activity:

2.5.1. Minimum inhibitory concentration (MIC)

The biological activities for the prepared ligand and its solid complexes were examined against diverse types of strains isolated from animal byproducts. These strains were suspected to be the main reason for food intoxication in human. Staphylococcus aureus, Bacillus

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