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SYNTHESIS AND CHARACTERIZATION OF BENZOCAINE SCHIFF BASE AND ITS COBALT COMPLEX

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ABSTRACT: Ethyl4-(2-hydroxy-benzylideneamino) benzoate Schiff base ($C_{16}H_{15}NO_3$), were synthesized and the structure was studied against the bases of X-ray, UV, visible, elemental analysis, ^{1}HNMR, IR and Mass spectroscopy. The crystal structure of the nickel complex has been determined by single crystal X-ray conformed the molecule, which indicate the compound is crystalline in the monoclinic C2 / c with a = 16.0916 (5) Å, b = 6.0315 (2) Å, c =29.0072 (10) Å, α = 90.00°, β= 101.856 (2)°, γ = 90.00°, V= 2755.3 (2) Å3 and Z = 8. Because of intra-molecular hydrogen bond involving the O atom of hydroxy group and N atom of azomethine group; the two benzene rings and azomethine group are practically coplanar. The Cobalt complex was prepared; the structure was characterized in the bases of IR spectra, elemental analysis, UV - visible, and conductance measurements. Also, the biological activity of both Schiff base and its Cobalt complex show that they are biologically active.

INTRODUCTION: Schiff bases, which have an azomethine (imine) group (-C=N-) are usually prepared by condensation of a primary amine with an active carbonyl compound usually aldehyde or ketone [1]. Schiff bases as chelating agents (ligands) in the field of coordination chemistry and their metal complexes are of great interest for many years; because O, N, and S atoms play a vital role at the active sites of numerous metallobiomolecules in the coordination chemistry of d-block elements [2] in addition of their biological applications as anticancer, antimicrobial [3], antifungal, antibacterial, and antiviral agents [4].

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Also, Schiff base metal complexes have been widely studied because they have industrial and herbicidal applications [5] antitubercular activities [6] and chelating abilities which give it attracted remarkable attention [7]. Benzocaine was prepared by direct esterification of p-aminobenzoic acid with absolute ethanol, in the presence of sulfuric acid as dehydrating agent [8]. In the present work, the Schiff base (ethyl 4-(2-hydroxybenzylidene-amino) benzoate) and its Cu complex were prepared and its X-ray crystal structure was studied. The structure of Schiff base and its Cu complex were conformed on the bases of elemental analysis, UV-VIS, IR, and molar ratio methods. The aim of this work is to synthesis a cobalt Schiff base, then confirm it Spectro chemically and study its biological activity.

MATERIALS AND METHODS:

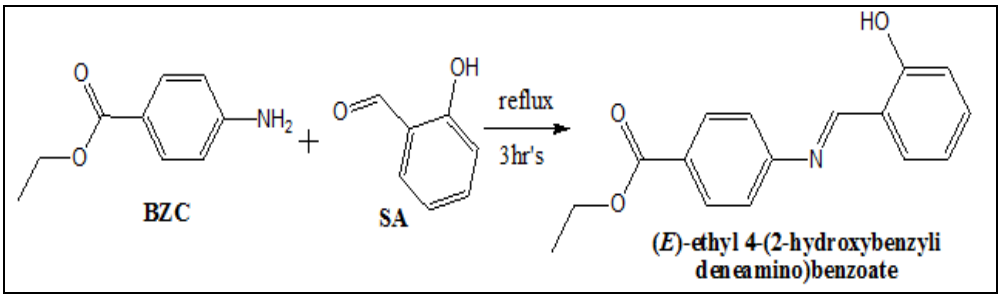
Materials: Benzocaine (BZC) (was obtained from pharco. Co. for pharm. Egypt) and salicylaldehyde (SA) was obtained from Morgan chemical IND,

Co, Egypt. Triethylamine (was obtained from Scharlau chemical, European Union), glacial acetic acid and absolute ethanol (was obtained from El-Nasr Pharmaceutical Co, Egypt), N, N-dimethyl form amide and diethyl ether (was obtained from Sd finne-chem.

Limited India, ethanol 99% (was obtained from Technolgene. Corp, Dokki, Egypt), Cobalt acetate were chemically pure of grade, Merck, Germany.

Instruments: For Schiff base (I) and its Cobalt complex (Ia); the electronic spectra were recorded by Perkin Elmer Lambda 35 Spectrophotometer using Dimethyl formamide as a solvent, IR spectrum were recorded on a Perkin Elmer spectrophotometer 57928 RXIFT-IR system,1H NMR spectrum of Schiff base was recorded by a Varian, USA, Gemini 200 MHz instrument using TMS as an internal standard and DMSO-d6 as a solvent, microanalysis for Schiff base and its Cobalt complex were carried out in the Micro Analytical Center, Cairo University-Egypt, Conductance TDS Engineered system, U.S.A, was employed for the conduct metric titration in Al-Azhar university, Egypt and the metal analyses were determined by atomic absorption (AAS Vario 6 in spectroscopy analytical lab. Faculty of Science, Al-Azhar University, Egypt.

Synthesis of Schiff Base (I): Schiff-bases (Scheme 1) was prepared by usual condensation reaction [9], by adding salicylaldehyde (0.1 mole) drop wisely to (0.1 mole) benzocaine with continuous stirring (drops of triethylamine [10, 11] and glacial acetic acid [1, 12] was added). After complete addition, the reaction refluxed for about 3 h. After cooling to room temperature, the products (imines) were separate by filtration. Recrystallization from ethanol. After one week orange prisms of compound (I) were obtained. Melting point equal to 82 ºC.



SCHEME 1: SYNTHESIS OF SCHIFF BASE (I)

Preparation of Schiff Base metal Complexes:

Molar Ratio:

Conductometric Titration and Molar Conductance Fig. 1: The conductometric titration is performed by titrating10 ml of 1x10-3 M Co (II) solution with the increasing volume of 1x10-3 M solution of Schiff base as a complexing agent, using DMF as a solvent, the conductance was recorded every two minutes.

By plotting the conductance value versus milliliter of the reagent added and applying the least square equation for Y values according to the following equation; Y= mX+b Where Y: is one variable, (conductance volume), X: the other, (volume of (L+P) solution), m: is the slope of the curve and b: is the intercept on the ordinate. (Y) is usually the measured variable plotted as a function of changing X.

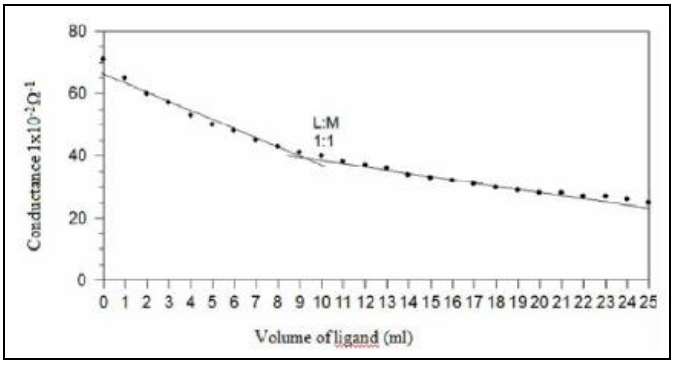


FIG. 1: CONDUCTOMETRIC TITRATION OF SCHIFF BASE (I) (1× 10^{-3}M) WITH (CH_3COO) 2CO. $4H_2O$ (1×10^{-3}M) SYSTEM

Spectroscopic Molar Ratio Testing: In the present work, the concentration of the metal ion was kept constant, while that of the Schiff base ligand was changed as it was published by J. Rydbarg. To a 2.0 ml of 1×10^{-3}M solution Co+2 ions adds the ligand with regularly varied solution

from 0.2×10-3 to 2×10^{-3}M using DMF as a solvent. The absorbency of the mixed solutions was measured. The results obtained are represented graphically in **Fig. 2.**

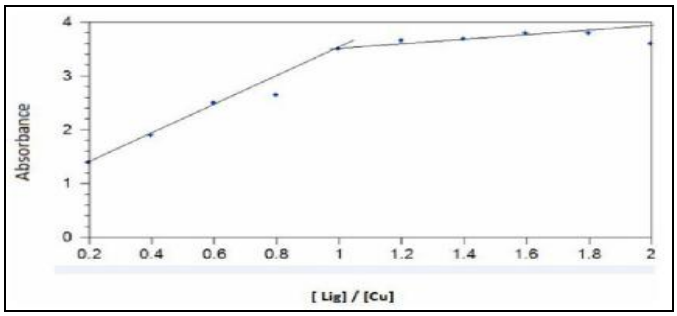
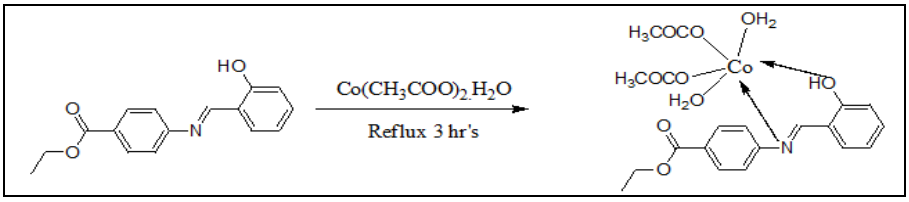


FIG. 2: ABSORPTION SPECTRA OF CO (II) COMPLEX MOLAR RATIO METHOD

Synthesis of Schiff base - Cobalt Complex: A 25 ml solution of the cobalt acetate Co $(CH_3COO)_2$. $4H_2O$ (0.001 mole) in absolute ethanol was added drop wise to equimolar amounts of Schiff base (I). After the complete addition of the metal salt the reaction mixture was heated under reflux for about four hours. Then, collect the product by filtration and recrystallization from ethanol to give solid products (I_a) (Scheme 2) with Yield = 48.26% (0.25 g). The m. p of the complex is 225 ºC. A plot of the absorbance as a function of molar ratio metal ion/ligand is represented by two portions, which indicate the formation of 1:1 complex. Elemental analysis revealed that the complex formed by interacting cobalt II acetate with the ligand is bidentate, and a water molecule should occupy the sixth position around the metal ion to satisfy coordination number 6.



SCHEME 2: SYNTHESIS OF SCHIFF BASE - COBALT COMPLEX (Ia)

RESULTS AND DISCUSSION:

The Structure of Schiff Base (I) was Elucidated on the Bases of:

Elemental Analysis: The elemental analysis: C, H, and Nof Schiff base (ethyl4-(2-hydroxy-benzylideneamino) benzoate) calculated (measured) were (71.36 (70.3), 5.61 (9.87), and 5.2 (5.12)) respectively.

The ^{1}H-NMR: The ^{1}H-NMRs pectrum of the Schiffbasein DMSO exhibits signals at ρ 11, 8.647, 4.4, and 1.4 ppm, attributed to -OH, -CH=N-, -CH_2 and -CH_3 protons, respectively. The multi-signals within the range at ρ= 6.95-7.79 ppm are assigned to the aromatic protons of both rings.

UV-Vis: UV-Vis in (DMF) as a solvent exhibits the absorption and structure atλ_{max}= 267 nm corresponds to π-π* transitions of the C=Ngroup. Thebroad band at λ_{max} = 332 nm corresponds to n-π* transitions of the azomethine and carbonyl groups.

The IR Spectrum: The IR spectrum exhibits a broadband in the region 3254 cm^{-1} characteristics to the stretching mode of vibrations of phenolic OH group. The region from 1700 to 1400 cm^{-1} exhibits two bands at 1590 cm^{-1} and1704 cm^{-1}. The band at 1590 cm^{-1} may be assigned as ν C=N stretching mode of vibration of the azomethine group [12, 13]. Asharp peak at 1704 cm^{-1} is due to C = Ostretching mode of vibrations. And stretching vibration of aromatic C=C at 1455 cm^{-1}. Finally, the bands at 2973, 2750, and 1361 cm^{-1} may be assigned as νC-Haromatic, C-Haliphaticand C-N respectively [13].

X-ray Crystal: X-ray crystal structure as in previous article [14] view of the asymmetric unit is shown in **Fig. 3**. The asymmetric unit contains one crystallographically independent Schiff bases.

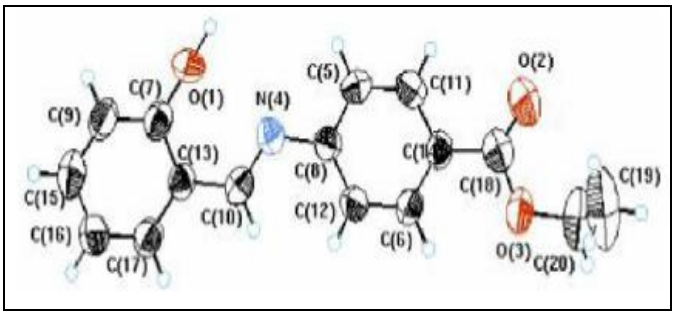


FIG. 3: ORTEP VIEW OF THE TITLE COMPOUND (I) SHOWING 30% PROBABILITY DISPLACEMENT ELLIPSOIDS

The Structure of the Co-complex of Schiff base (I) was elucidated on the bases of:

The Element Analysis: The results of nitrogen and metal were compatible between calculated and measured, respectively, 2.7 (2.4) and 11.37 (9.8).

Electronic Spectra: The electronic spectra of the Schiff-base complexes were carried out in DMF solutions at a concentration of 10^{-5} - 10^{-3} M. The spectrum of the complex exhibits the absorption band structure at λ_{max} = 225, and 262 nm corresponds to π-π* transitions of the C=O and C=N groups respectively. The sharp band at λ_{max} = 315 nm corresponds to n- π* transitions of the acetate group. The sharp band at λ_{max} = 383 nm corresponds to n- π* transitions of the azomethine group. Where the band at λ_{max} = 389-410 corresponds to d - d transitions of the cobalt metal.

IR Spectra: The IR spectrum exhibits broadband at 3436 cm^{-1} instead of 3254 cm^{-1} in Schiff base, characteristic of the stretching mode of vibrations of phenolic OH group. The region from1700 to 1400 cm^{-1} exhibits two bands at 1601 instead of 1590 cm^{-1} and 1709 cm^{-1} instead of 1704 cm^{-1}; the band at 1601 cm^{-1} may be assigned as ν C=N stretching mode of vibration of the azomethine group [12, 13]. A sharp peak at 1709 cm^{-1} is due to C=O stretching mode of vibrations. The stretching vibration of aromatic C = C at 1445 cm^{-1}. Finally, the bands at 2978 instead of 2973 and 1370 instead of 1361 cm^{-1} may be assigned as ν C-HAr and C-N respectively [14], as a result of the Co complex (I_a); the absorption of all bonds increase than that of a Schiff base.

Biological Activity: The antibacterial and antifungal activity of the Schiff base (I) and its cobalt complex (I_a) was done in comparison with penicillin g and streptomycin for antibacterial clotrimazole and itraconazole for antifungal as standard.

All the 6 selected strains tow of bacteria and four of fungi, namely; {Pseudomonas aeruginoca and Escherichia coli (Gram-) and *Staphylococcus aureus* and Bacillus (Gram +) and *Aspergillus fumigates*, *Candida albicans*, *Geotrichum candidum* and *Syncephala strumracemosum*} showed sensitivity to all derivatives and compound I and I_a has shown good activity against all the tested fungal and bacterial except syncephala strumracemosum.

CONCLUSION: Ethyl 4 - (2 - hydroxyl - benzy-lideneamino) benzoate (Schiff base (I)) was synthesized from the reaction between mixture of benzocaine and o-hydroxybenzaldehyde, the Schiff base (I) reacted with cobalt acetate tetrahydrate and the resul to fall previous physiochemical measurements show that the structure of 1:1 complex may be represented as in Scheme 2. The Schiff base behaves as bidentate ligand one from hydroxyl oxygen and the other from azomethine nitrogen, to form an octahedral structure. Finally, the two compounds I and I_a show more effect on both bacterial and fungal than the basic drug (benzocaine).

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Ethical Approval: There is no need for ethical approval because we did not apply my study on animals or humane.

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