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RESEARCH ARTICLE

Synthesis, Spectral Characterization, Theoretical Evaluation of New Cu (II) and Ni (II) Complexes of Flavon

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Abstract

A new series of Cu (II) and Ni (II) complexes with the Flavone ligand were prepared and spectroscopic method and elemental analysis verified their structures. All the prepared complexes have been identified by available spectroscopic tools (UV-Visible and IR) in addition the structure of complexes was characterized by magnetic moments and molar conductance in DMSO solution .From the above of these studies and measurements suggest an tetrahedral geometry around Cu(II) and Ni(II). A theoretical treatment of the formation of complexes in the gas phase was studied; this was done using the Hyperchem-6 program for the Molecular mechanics and Semi-empirical calculations.

Keywords: *Flavone, Metal complexes, Synthesis, Spectral, Theoretical Evaluation.*

Introduction

Flavonoids represent one of the largest groups of natural products. In addition to the various functions of flavonoids in plants, their widespread distribution in nature, their structural variability, their relatively low toxicity, and their antioxidant activities have increased the interesting flavonoids as beneficial for human health. Several therapeutically interesting biological activities of certain flavonoids have been reported including antibacterial[1] , antiviral, anti-inflammatory [2,3], anti-allergic [4], antithrombotic [5], anti-mutagenic, anti-neoplastic [6], neuro protective properties [7], and antioxidant properties[8,9], etc.

The biological activity of flavones can be modified upon formation of metal complexes [10]. Flavonoid-metal complex compounds are the subject of our longtime research during which we investigated properties, composition, complex formation features, stability constants, as well as analytical appraisal of approximately 40 complexes of flavonoids from different flavonoid subclasses with a number of metal ions or metal groups [11].

The biological effects of flavonoid-metal complexes, confirmed by other authors in numerous studies, showed that complexes are more effective then free flavonoids.

All these data are available in various previous publications [12, 13]. The newly synthesized flavone (L) and their metal complexes [14] were characterized by elemental, spectral analysis (IR, UV-Vis.).

Experimental

Instrumentation and Chemical

IR spectra were recorded Pye Unicam Sp. 3100 spectrophotometer; solid samples were measured as KBr disc. For UV measurement absolute methanol and ethanol were used as solvents. Rotary evaporator RE-120 Buchi. Gallenkamp (hot stage) determined M.P. Perkin Elmer B-240 was used for the metal analysis. BDH chemicals Ltd.-England, Fluka AG Buchs-Swaziland and Riedel Du Haen Germany supplied chemicals.

General Procedure for the Preparation of Chalcone, (E)-1-(2-hydroxyphenyl)-3-(4-hydroxyphenyl) Prop-2-en-1-one (1)

To the mixture of o-dihydroxy acetophenone (13.6 gm, 0.1 mol), alcohol (50 mL) and p-hydroxy benzaldehyde (12.72 gm, 0.12 mol), NaOH (40%,19mL)was slowly added with vigorous stirring (2-3 hrs), till orange solid mass was obtained and left it overnight at ambient temperature. Cold 5N, 42 mL HCl was poured on to it with constant stirring.

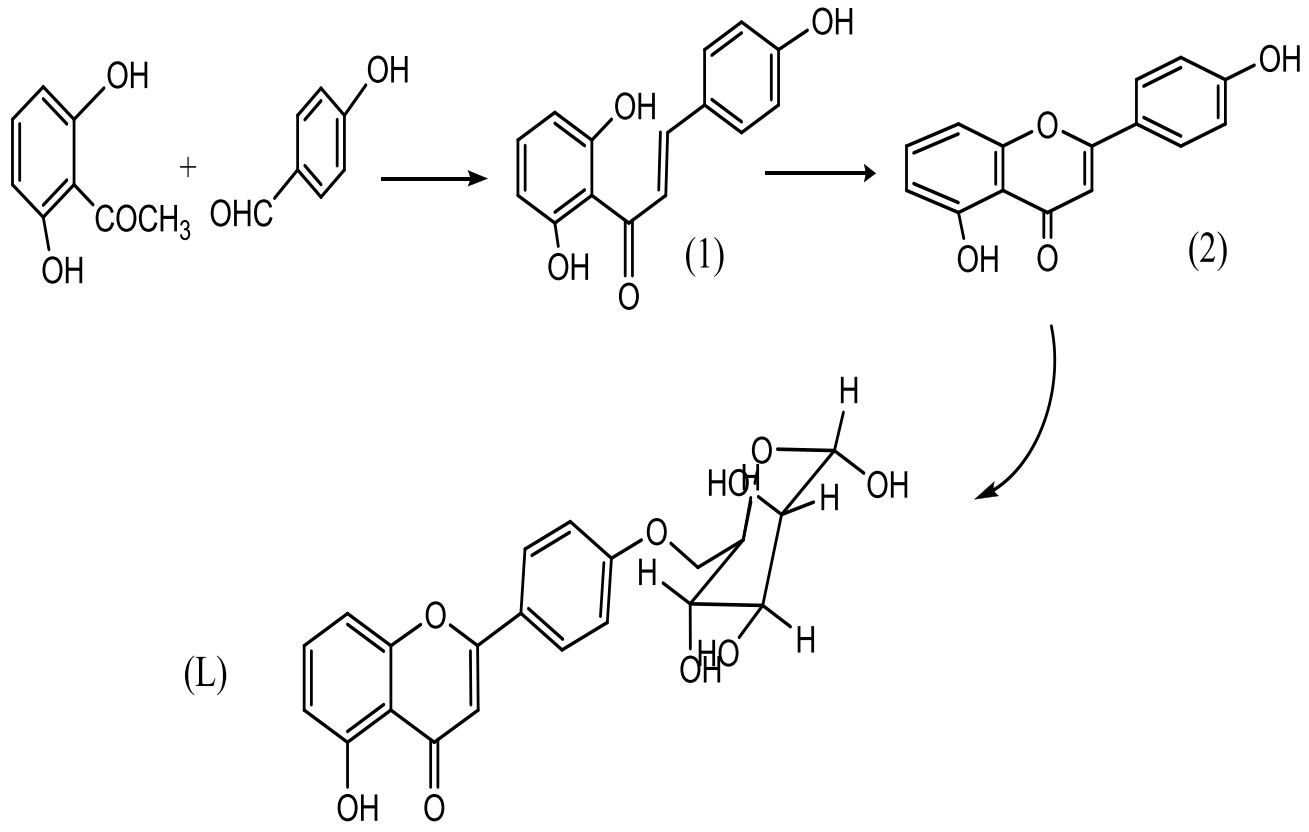
The yellow solid was filtered, washed with water, dried and crystallized from alcohol. Yield 80%, brownish red powder, M.P. >240 ºC, IR (KBr disc) shows absorption at 3412 cm^{-1} (OH), 1655 cm^{-1} (C=O). UV-Vis shows max (EtOH) 295 nm, 354 nm. C. H. N. analysis; C=69.95 (cal. 70.03), H=5.12 (cal. 5.09).

General Procedure for the Preparation of Flavone, 5- hydroxy- 2- (4-hydroxyphenyl)-4 H- chromen- 4- one (2)

The mixture of (E)-1-(2-hydroxyphenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (1) (2.40 gm, 0.01 mol),ethanol (50 mL), Noah (10%, 56 mL) and H_2O_2 (30%, 13 mL) was stirred vigorously for 30 minutes and kept for 4 hrs at ice cold condition. It was poured on to cold 5N, 80 mL HCl. The solid was filtered, washed with water, dried and crystallized from alcohol (yield 75%); mp >240 °C; FT-IR (KBr): 3426 (Ar-OH), due to presence of phenolic –OH group, 3075 (aromatic str.), 1641 (C=O pyrone ring) cm^{-1}; UV-Vis shows max (EtOH) 260 nm, 311 nm and 352 nm. C. H. N. analysis cal. C, 66.89; H , 4.76 %.Found: C, 66.71; H, 4.53%.

General procedure for the preparation of Flavone-Mannose, 5-hydroxy- 2-(4-(((2R, 3S, 4S, 5S, 6S)-3, 4, 5, 6-tetrahydroxytetrahydro-2 H- pyran-2-yl) methoxy) phenyl)- 4H- chromen-4-one (L)

Take (1 mol) of Flavone 5-hydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one (2) and dissolved in (200ml) of DMSO and placed inside round flask capacity (100ml) then add (1 mol) of dissolved Mannose in (20ml) of the same solvent and added drops of (5%) of HCl, the mixture heated for two hours in a water bath and then the solvent is evaporated and collects the output. spectral data of these compounds are given as follows: (yield 65%); FT-IR (KBr): 3401 (Ar-OH), due to presence of phenolic –OH group, 1600 (C=O pyrone, ring) cm–1; UV-Vis shows max (EtOH) 250 nm, 280 nm and 350 nm. C. H. N. analysis cal. C, 60.58; H, 4.84%.Found: C, 60.71; H, 4.33%.



Scheme 1: Synthesis of Ligand

General Procedure for the Preparation of the Complexes

0.2 mmoles from L ($C_{21}H_{20}O_9$) was dissolved in MeOH (30 ml) then 0.1 mmole metal chlorides was added. The resulting mixture was refluxed for 30 min. and the volume of the final mixture was reduced under vacuum. The crude products were purified by recrystallization from MeOH to give a powder, yield 82%. The complexes are listed in Tables (1, 2).Fig. 1.

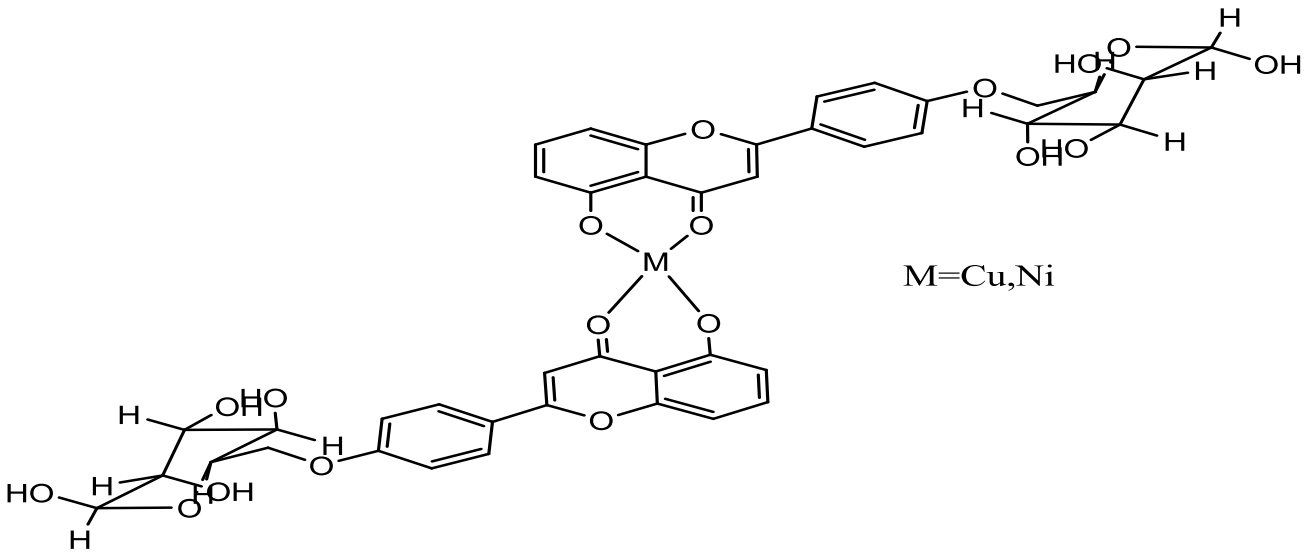


Fig. 1: Suggested structure of the Cu (II) and Ni (II) complexes

Result and Discussion

Claisen Schmidt condensation was chosen for the synthesis of chalcone (1). The reaction partners are 2-hydroxy acetophenone and benzaldehyde, which condense in the presence of base in aqueous alcoholic solution. The flavone have been synthesized through on cyclization in alkaline H_2O_2 yielded5-hydroxy-2- (4-hydroxyphenyl)- 4H-chromen-4-one (2), which react with mannose to produce, 5-hydroxy-2-(4- (((2R, 3S, 4S, 5S, 6S)- 3, 4, 5, 6-tetrahydroxytetrahydro-2H-pyran-2-yl)methoxy)phenyl)-4H-chromen-4-one (L) (Scheme 1).

Complexes formation between Cu(II) or Ni(II) chlorides and 5-hydroxy-2-(4-(((2R, 3S,4S, 5S,6S)-3 ,4 ,5, 6-tetra hydroxytetrahydro-2H-pyran-2-yl) methoxy) phenyl)-4H-chromen-4-one(L) performed in ethanolic dimethylformamide show the formation of mononuclear complexes with 1:2 metal to ligand stoichiometry (Fig 1). The complexes are stable at room temperature, non-hygroscopic, insoluble in water but slightly soluble in chloroform and soluble in DMF and DMSO. Prepared ligands have been characterized by spectroscopic methods (UV-Vis, IR) and C. H. N. analysis.

FT-IR Spectra

The characteristic infrared spectral assignment of ligand (**L**) and their complexes are reported in experimental section. In the FT-IR spectra of ligand (**L)**, the presence of phenolic OH and carbonyl group are confirmed by peaks at 3401 and 1600 cm-1respectively [15]. However, in the spectra of the complexes there is complete disappearance of peak at 3401 cm-1 suggesting absence of phenolic OH group indicates its coordination.

The band assigned to the carbonyl group is shifted to a lower wave number comparing with that of the free ligand, proving its coordination. Supplementary bands around 524-534 cm-1 for complex is assigned to the ν (M-O) [16]. As a conclusion, comparison of the spectra of ligands and metal complexes conform the coordination of ligand to metal ion, bidentately through the 3-hydroxy 4-keto groups (Table 2).

UV-Vis Spectra

The UV-Vis spectra of the complexes expected differences in the position of the absorption bands between the ligands and the related complexes, which are due to the coordination between the ligands and the transition metals. Appearance of new absorption maxima is considered as a hint for the formation of complexes. The bathochromic shift in band I upon coordination is due to the electronic transition (n→π*) of the lone pair of electrons of the hydroxyl group in the complex (Table 2). Band II, which caused by the transition (π→π*) of the aromatic ring, exhibit absorption maxima at 280 nm.

This measured wavelength reflects the effect of substitution by auxochromes (hydroxyl group) caused a bathochromic shift in bands I and II, of the complexes [14]. From the above spectroscopic results (IR, UV-VIS) and atomic

absorption the following general structure can be proposed for the metal–Flavone complexes.

Conductivity Measurements

The measurements of the molar electrical conductivity of the complexes in DMSO are indicated in Tables (2). These results clearly show values for the molar conductivity of the complexes of bivalent metals are non-electrolyte.

PH Effect Study

The complex was dissolved in methanol and buffer solution was added, a hypsochromic shift was noticed in case of decreasing pH as shown in Fig.(2).the absorption maximum in the UV-Vis. Spectra of complex Cu(II) was monitored at different pH values, from 2.0 to 12, obtained through titration with NaOH (0.01 mol/L) or HCl (0.01 mol/L) solutions.

No change in the maxima was observed. This shows that the changes in the pH of the solution do not lead to the dissociation of the metal from the flavonoid, but below pH =2 (strong acidic medium) the complexes are unstable and a stable complex has been observed in higher pH-values (pH=8).

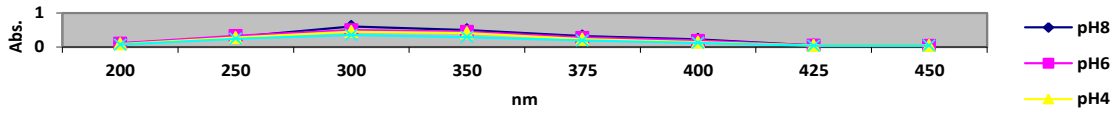


Fig. 2: UV-Vis. Spectra of Cu (II) complex at different pH values

The Molar-Ratio Study

The mole-ratio [17a, b] is one of the most common spectrophotometric techniques employed in complex studies. It is an available tool for elucidating the composition of complex in solution. Molar-ratio (2:1) of ligand (L) to the metal (Cu (II)) is effected by the absorption due to change in coordinate ion of the ligand complexes as shown in Fig. (3).

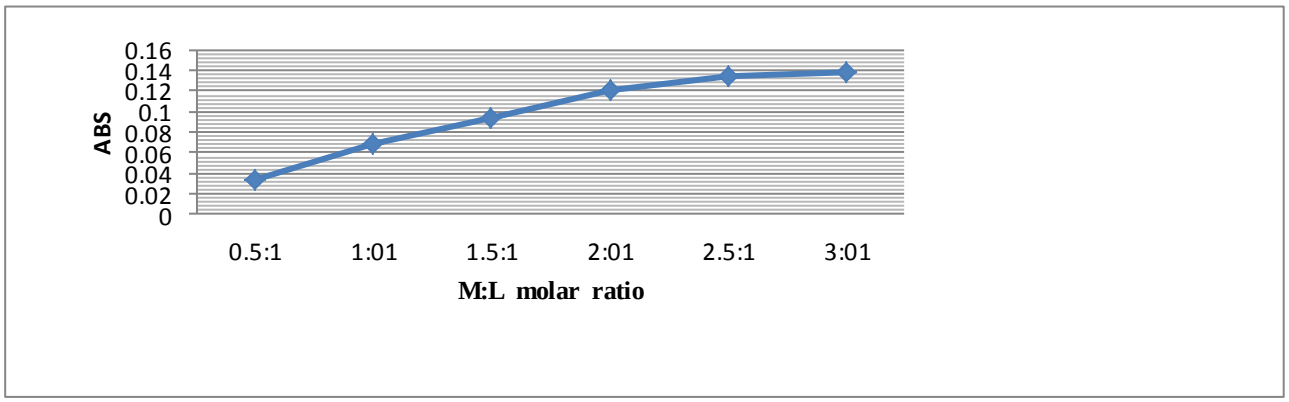


Fig. 3: Plot of the Cu (II) complex formation

The Magnetic Moments

The magnetic moments of divalent Nickel, and Copper complexes at 3.15 and 1.48BM ranges respectively at room temperature and are close to the predicted value for tetrahedral geometry around the metal atom [14a,b].

Theoretical Study

The ball and cylinders and some of selected structural parameters (bond length and angles) of the optimized geometries are shown in Table (3), Fig.(4). As shown in this figure, there is no obvious trend for the variation of these parameters. The values of the bond length and angles of the optimized geometries are quite similar to the experimental results of the corresponding compounds [18].

Fig.4: The optimized structural geometry of Cu (II) complex

Complex Formation and Stability Constant

According to the literature, the most reliable results of the stoichiometric composition of flavonoid complexes were obtained by the method of continual variation of equimolar solutions [17]. Consequently, the stoichiometry of the complex in methanol solution was investigated using both Jobs method and the slop ratio method [18]. When we plotting the absorbance versus mole fraction of ligand, the results indicated that 2:1 chelate is formed. The results were consistent with data obtained using slop ratio method. To determine the apparent stability constant of the complex, absorption spectra of solution containing 2:1 L: M were recorded Fig.3. The stability constants K_f were calculated as $1.48x10^3$and $2.66x10^3$ for Cu (II) and Ni (II) complexes, which is in agreement with Irving- Williams [19] order of stability constants of bivalent metal complexes.

Table 1: Micro Elemental analysis (C.H.N.M) data of ligand

compound	M.p. C°	color	%C Calc. (Found)	%H Calc. (Found)	%Metal Calc. (Found)
[Ni(L)$_2$]	>240	Pale green	56.72 (56.33)	4.31 (4.61)	6.60 (6.51)
[Cu(L)$_2$]	>240	blue	56.41 (56.88)	4.28 (4.87)	7.11 (7.03)

Table 2: Infrared spectral bands, electronic spectra, magnetic moments and molar conductance of the prepared complexes

compound	IR, (cm^{-1})			λ_{max} (nm)	assignment	$\mu_{eff.}$ BM	*ΔM (Ω^{-1} cm^2mol^{-1})
	υ (C=O)	υ(OH)	υ(M-O)				
L	1600(s)	3401 (m)	-	350, 280 250	n→π*, π →π*	-	-
[Ni(L)$_2$]	1575(s)	3375 (m)	524	259, 297, 377	$^3T_{1\,(F)} \rightarrow {}^3T_{1\,(P)}$ $^3T_{1\,(F)} \rightarrow {}^3A_{2(F)}$ $^3T_{1\,(F)} \rightarrow {}^3T_{2\,(F)}$	3.15	7
[Cu(L) $_2$]	1584(s)	3370 (br)	534	265, 300, 490	$^2B_1g(F) \rightarrow {}^2B_1g(F)$ $^2B_2g^2(F) \rightarrow {}^2A_2g(p)$ C.T	1.84	9

br=broad, s=strong, and m=medium , *=molar conductance in 0.001M solutions in DMSO,C.T=charge transfer of L to M type

Table 3: Structural parameters, bond length (ºA) and angles (º) of the [Cu (L) $_2$] complex

Parameters		Parameters	
Bond lengths (ºA)		**Bond angles(º)**	
O(53)-Cu(71)	3.1066	C(38)-O(53)-Cu(71)	113.7289
O(43)-Cu(71)	1.8100	C(44)-O(43)-Cu(71)	179.9996
O(18)-Cu(71)	1.8100	O(8)-Cu(71)-O(18)	88.3235
O(8)-Cu(71)	1.8007	O(8)-Cu(71)-O(43)	109.4998
C(3)-O(18)	1.3550	O(8)-Cu(71)-O(53)	135.1016
C(3)-C(4)	1.3370	O(18)-Cu(71)-O(43)	109.5001
C(2)-H(73)	1.1000	O(18)-Cu(71)-O(53)	65.7436
C(2)-C(3)	1.3370	O(43)-Cu(71)-O(53)	53.7876
C(1)-H(72)	1.1000	C(9)-C(10)-C(11)	121.8274
C(6)-C(1)	1.3370	C(9)-O(8)-Cu(71)	104.5939
C(1)-C(2)	1.3370	C(3)-O(18)-Cu(71)	109.5001
C(9)-O(8)	1.2080	C(1)-C(2)-H(73)	120.0004
O(7)-C(11)	1.3550	C(3)-C(2)-H(73)	120.0003
C(6)-H(74)	1.1000	C(2)-C(1)-C(6)	120.0007
C(5)-O(7)	1.3550	C(2)-C(1)-H(72)	119.9998
C(5)-C(6)	1.3370	C(6)-C(1)-H(72)	119.9994

Conclusion

The available experimental data suggest that the prepared L possesses two coordinating sites as bi dentate ligand. Physical and spectroscopic characterization of the complexes revealed that the OH group and carbonyl group of flavone were involved in the coordination and that the Ni (II) and Cu (II) had tetrahedral geometry. Generally, antimicrobial activity is due to the oxygen atom and substituted benzene ring system.

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