



Synthesis, Characterization, Theoretical and Antimicrobial Evaluation of New Mn(II), Cu(II) and Zn(II) Complexes of Flavylum Salt

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Abstract: A new series of Mn(II), Cu(II) and Zn(II) complexes with the two ligands were prepared and spectroscopic method and elemental analysis verified their structures. The first ligand L1 is flavylum salt and the second L2 is a Flavon. Reaction between transition metal salts and the ligands have synthesized two groups of new metal complexes. These complexes have been identified by available spectroscopic tools (UV-visible and IR) the C.H.N results confirmed the proposed structures. The experimental data disclosed that the complexes were coordinated by 6-the coordinate with mono- and bidentate ligands forming octahedral structure, in which L2 acts as monodentate and L1, L2 as bidentate ligands. The metal linked with L1 through the oxygen in ortho position in ring B, were as the linkage of the metal with L3 takes place through the oxygen of the carbonyl group. 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. The antimicrobial activity of the ligand and its metal complexes were studied against the following strains of microorganism: Staphylococcus aureus and Escherichia coli by the well diffusion method. Metal complexes showed enhanced antimicrobial activity compared with that of the free ligand.

Keywords: Flavylum Salt, Flavon, Metal Complexes, Antimicrobial Activity

1. 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, the irrelatively low toxicity, and their antioxidant activities have increased the interesting flavonoids as beneficial for human health.

Hayashi et al [1] extracted a blue anthocyanin (commelinin) from the petals and found it to contain Mg. Flavone like substance and awobanin (delphinidin 3-p-6-commaroyl glucoside-s-glucoside) Abathochromic shift have been observed in the UV spectrum by Asem [2], when Aluminum chloride was added which indicates the formation of Aluminum-cyanodin complexes. Many metal complexes with different type of anthocyanins have been prepared later by other workers [3]. The structure of metal complexes depends upon the ratio of ligands to metal and to the

Oxidation State of the metal ion. Evidence of the structure and bonding state of the commelinin metal was provided by ESR studies of Mg complexes, electrophoreses and IR spectra [3, 4].

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 [6, 7]. The biological effects of flavonoid-metal complexes, confirmed by other authors in numerous studies, showed that complexes are more effective than free flavonoids. All these data are available in various previous publications [8, 9].

The synthesized flavone and their metal complexes were characterized by elemental, spectral analysis (IR, UV-Vis.).

2. Experimental

2.1. Instrumentation and Chemical

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. Atomic absorption spectra on Shimadzu AA-680. 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.

2.2. General Procedure for the Preparation of Ligands

The flavylum chloride 2-(3,4-dihydroxyphenyl)chromenylium (L1), (Fig. 1) was prepared as described in the literature [10].

3-acetoxy-2-(3,4-dihydroxyphenyl)chromenylium (L1):

Brownish red powder, m.p. 115-116°C, yield 84%, IR (KBr disc) shows absorption at 3400 cm^{-1} (OH), 1680 cm^{-1} (C=O). UV-Vis shows max (EtOH) 494 nm, 274 nm, C. H. N. analysis; C=65.52 (cal. 65.58), H=4.02 (cal. 4.04).

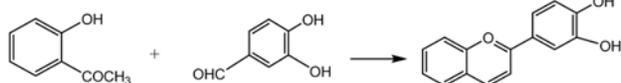


Fig. 1. Synthesis route to the ligand 2-(3,4-dihydroxyphenyl)chromenylium (L1).

2.3. General Procedure for the Preparation of Chalcone, (E)-1-(2-Hydroxyphenyl)-3-(4-Hydroxyphenyl)Prop-2-en-1-One (1)

To the mixture of 1-(2-hydroxyphenyl)ethanone (13.61 gm, 0.1 mol), alcohol (50 mL) and p-hydroxy benzaldehyde (12.72 gm, 0.12 mol), NaOH (40%, 19 mL) 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°C, IR (KBr disc) shows absorption at 3410 cm^{-1} (OH), 1650 cm^{-1} (C=O). UV-Vis shows max (EtOH) 290 nm, 340 nm. C. H. N. analysis; C=74.95 (cal. 74.99), H=5.02 (cal. 5.03).

2.4. General Procedure for the Preparation of Flavone, 2-(4-Hydroxyphenyl)-4H-Chromen-4-One (2)

The mixture of (E)-1-(2-hydroxyphenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (1) (2.38 gm, 0.01 mol), ethanol (50 mL), NaOH (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): 3430 (Ar-OH), due to presence

of phenolic -OH group, 3070 (aromatic str.), 1640 (C=O pyrone ring) cm^{-1} ; UV-Vis shows max (EtOH) 260 nm, 311 nm and 352 nm. C. H. N. analysis cal.; C, 75.62; H, 4.23%. Found: C, 75.59; H, 4.21%.

2.5. General Procedure for the Preparation of Flavone – Mannose, 2-(4-(((2R,3S,4S,5S,6S)-3,4,5,6-Tetrahydroxytetrahydro-2H-Pyran-2-yl)Methoxy)Phenyl)-4H-Chromen-4-One (L2)

Take (4.0 gm, 1 mol) of Flavone 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): 3400 (Ar-OH), due to presence of phenolic -OH group, 1605 (C=O pyrone ring) cm^{-1} ; UV-Vis shows max (EtOH) 255 nm, 275 nm and 350 nm. C. H. N. analysis cal.; C, 63.00; H, 5.03%. Found: C, 62.97; H, 5.0%.

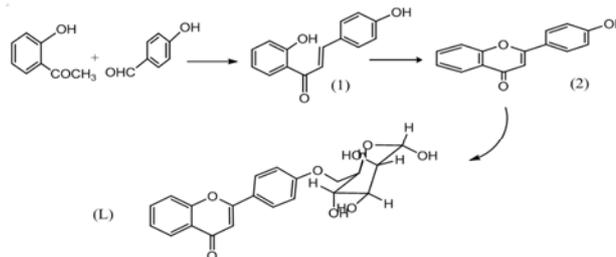


Fig. 2. Synthesis route to the ligand 2-(3,4-dihydroxyphenyl)chromenylium (L2).

2.6. General Procedure for the Preparation of the Complexes

0.2 mmoles from L1 ($\text{C}_{15}\text{H}_{11}\text{ClO}_3$) was dissolved in MeOH (30 ml) then 0.1 mmole metal chlorides was added. The mixture refluxed for 20 min during this time the solution became dark. A solution of L2 ($\text{C}_{21}\text{H}_{20}\text{O}_8$) in methanol (0.2 mmole) was poured to the dark solution. 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. 3.

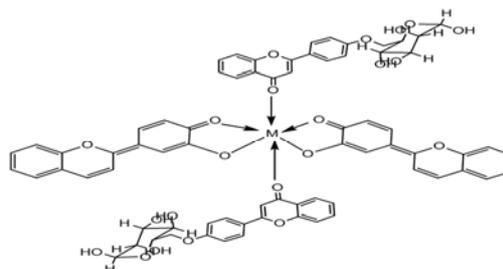


Fig. 3. Suggested structure of the Cu(II), Mn(II) and Zn(II) complexes.

2.7. Study of Biological Activity for Ligands and Their Metal Complexes

The biological activity of the ligands and their metal complexes were studied against two selected type of bacteria which included *Escherichia coli*, as gram negative (-Ve) and *Staphylococcus aureus* as gram positive (+Ve) to be cultivated and as control for the disc sensitivity test (11). This method involves the exposure of the zone of inhibition toward the diffusion of microorganism on agar plate. The plates were incubated for 24 hours at 37°C, the zone of inhibition of bacteria growth around the disc was observed.

3. Result and Discussion

The flavylum chlorides L1 and L2 have been synthesized according to the method devised by Robinson et al [10], through the condensation of O-hydroxy benzaldehyde with substituted acetophenone followed by ring closure with anhydrous hydrogen chloride Fig. (1). 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 H₂O₂ yielded 2-(4-hydroxyphenyl)-4H-chromen-4-one (2), which react with mannose to produce, 2-(4-(((2R,3S,4S,5S,6S)-3,4,5,6-tetrahydroxytetrahydro-2H-pyran-2-yl)methoxy)phenyl)-4H-chromen-4-one (L2) (Fig. 2). The analytical data of the complexes are given in table (1, 2). The found values were in good agreement with the theoretical ones, and correspond well with the general formula [M(L1)₂(L2)₂], where M=Cu(II), Co(II) and Ni(II). Complexes formation between metal chlorides and L1, L2 performed show the formation of complexes with 1:2:2 (M:L1:L2) stoichiometry (Fig 3). All prepared ligands and their complexes have been characterized by spectroscopic methods (UV-Vis, IR) and C. H. N. analysis.

3.1. IR Spectra

The IR spectra exhibit the expected absorption bands of the Flavylum chlorides (L1) and Flavon (L2). In the case of the complexes, in which L2 is involved, the carbonyl stretching frequency decreases to the range (1650-1630 cm⁻¹), due to the electron transfer from the ligand to the metal [11]. The evidence for the linkage of the metal to ring B in the flavylum complexes depends on the observation that an intensive band at 1620-1610 cm⁻¹ was observed. This band is due to the conjugation between the C=C and C=O which occur during the chelation [11]. The flavylum-metal complexes characteristic peak at 1265 cm⁻¹ for C-O (phenol). The -OH stretching band at 3400 cm⁻¹ appear broad with dimensioned intensity This finding has lead us to the conclusion that the metal was linked to ring B in each of the to flavylum ligand and the band assigned to the carbonyl group is shifted to a lower wave number comparing with that of the free ligand, proving its coordination. Table (2)

Supplementary bands around 520-540 cm⁻¹ for complex is assigned to the $\nu(M-O)$ and. 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).

3.2. 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 ($n \rightarrow \pi^*$) of the lone pair of electrons of the hydroxyl group in the complex Table (2).

Band III, which caused by the transition ($\pi \rightarrow \pi^*$) of the aromatic ring, exhibit absorption maxima at 285 nm. This measured wavelength reflect the effect of substitution by auxochromes (hydroxyl and methoxyl group). Replacement of chloride in L1 by acetate group caused a bathochromic shift in bands I, II, and III of the complexes [12].

3.3. Conductivity Measurements

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

3.4. The Magnetic Moments

The magnetic moments of divalent Mn and Cu complexes at 5.87 and 1.78 BM ranges respectively at room temperature and are close to the predicted value for octahedral geometry around the metal atom [12].

3.5. 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.

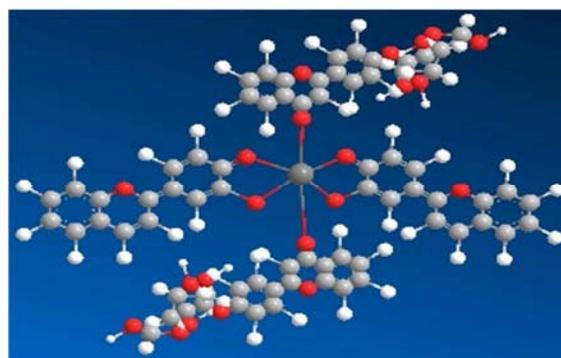


Fig. 4. The optimized structural geometry of Cu(II) complex.

3.6. Antibacterial Activity

The antibacterial activity of the ligand and its complexes were tested against the following stains of bacteria: *Staphylococcus aureus* and *Escherichia coli* by the well diffusion method [13]. The test solutions were prepared in DMSO, nutrient agar was used as the culture medium. The zone of inhibition was measured in mm and the values of the investigated compounds are summarized in Fig. (5).

The values indicate that the metal complexes had a higher antibacterial activity than the free ligand. Such increased activity of the metal complexes can be explained on the basis of the overtone concept and chelation theory [14].

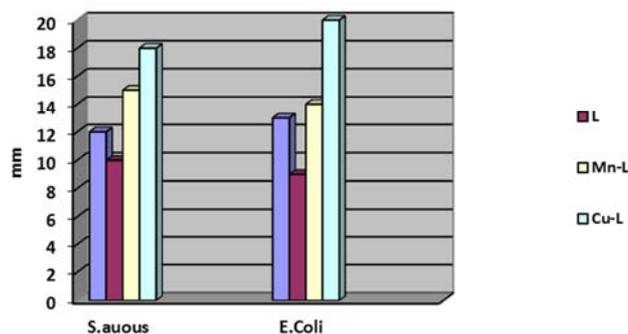


Fig. 5. The effect of ligand and their metal complexes toward bacteria.

Table 1. Physical characterization, analytical and Molar Conductance data of the compounds.

Compound	Yield %	Colour	$\Delta M/S \text{ cm}^2 \text{ mol}^{-1}$ In DMSO	μ_{eff} (BM)	Metal analysis (% found)% cal
[Mn(L1) ₂ (L2) ₂]	73	brown	11	5.87	(4.06) 4.13
[Cu(L1) ₂ (L2) ₂]	80	brown	9	1.78	(4.69) 4.75
[Zn(L1) ₂ (L2) ₂]	70	Pale-yellow	8	-	(4.82) 4.88

Table 2. Infrared and UV-Visible Spectra data of the prepared compounds.

Compound	UV-Visible Spectra (nm)	IR Spectra (Cm ⁻¹)		
		$\nu^{(C=O)}$	$\nu^{(C-O)}$	$\nu^{(M-O)}$
[Mn(L1) ₂ (L2) ₂]	280,310,440	1640	1245	525 m
[Cu(L1) ₂ (L2) ₂]	290,320,490	1630	1250	540 w
[Zn(L1) ₂ (L2) ₂]	285,303,426	1645	1255	530 m

Table 3. structural parameters, selective bond length (Å) and angles(°) of the [Cu(L1)₂(L2)₂] complex.

Parameter			
Bond lengths (Å)		Bond angles(°)	
C(39)-C(40)	0.6808	O(35)-C(32)-C(31)	123.6243
C(38)-H(124)	1.1000	C(33)-C(32)-C(31)	118.3440
C(43)-C(38)	0.6808	C(80)-O(79)-Cu(37)	179.3190
C(38)-C(39)	0.6295	C(46)-O(45)-Cu(37)	179.2585
O(79)-Cu(37)	2.9501	Cu(37)-O(36)-C(33)	109.0400
O(45)-Cu(37)	2.3182	Cu(37)-O(35)-C(32)	123.2588
O(36)-Cu(37)	1.6731	O(79)-Cu(37)-O(45)	175.8538
O(35)-Cu(37)	1.7415	O(79)-Cu(37)-O(36)	44.1878
C(34)-H(123)	1.0999	O(79)-Cu(37)-O(35)	111.9466
C(33)-C(34)	0.9209	O(79)-Cu(37)-O(18)	55.1822
C(33)-O(36)	1.2649	O(79)-Cu(37)-O(17)	113.8390
C(32)-O(35)	0.9209	O(45)-Cu(37)-O(36)	131.8218
C(32)-C(33)	0.8711	O(45)-Cu(37)-O(35)	63.9449
C(31)-H(122)	1.1000	O(45)-Cu(37)-O(18)	128.9640
C(19)-C(20)	0.8711	O(45)-Cu(37)-O(17)	70.3072
O(18)-Cu(37)	2.0012	O(36)-Cu(37)-O(35)	68.2190
O(17)-Cu(37)	2.0213	O(36)-Cu(37)-O(18)	98.0355
C(16)-H(114)	1.1000	O(36)-Cu(37)-O(17)	154.3836
C(16)-C(15)	0.9615	O(35)-Cu(37)-O(18)	165.5069
C(15)-O(18)	1.3685	O(35)-Cu(37)-O(17)	133.6211
		O(18)-Cu(37)-O(17)	58.6568
		Cu(37)-O(17)-C(14)	131.7803
		Cu(37)-O(18)-C(15)	114.0028
		C(16)-C(15)-O(18)	124.4690
C(14)-O(17)	0.9617		

3.7. Conclusion

The available experimental data suggest that the prepared L1 possesses two coordinating sites and L2 as monodentate ligand. Physical and spectroscopic characterization of the

complexes revealed that the OH group of the flavylum and carbonyl group of chalcone were involved in the coordination and that the Mn(II), Cu(II) and Zn(II) had octahedral geometry. Generally, antimicrobial activity is due to the oxygen atom and substituted benzene ring system.

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