



Synthesis, spectral characterization, theoretical evaluation of new Cr(III) and Fe(III) complexes of flavon

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ABSTRACT

A new series of Cr(III) and Fe(III) 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 octahedral geometry around Cr(III) and Fe(III). 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.

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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], antiallergic[4], antithrombotic [5], antimutagenic, antineoplastic[6], neuroprotective properties [7], and antioxidant properties[8,9], etc. The biological activity of flavones can be modified upon formation of metal complexes.

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 [10,11]. 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 [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. 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.

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%, 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 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)-4H-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), NaOH (10%, 56 mL) and H₂O₂ (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%.

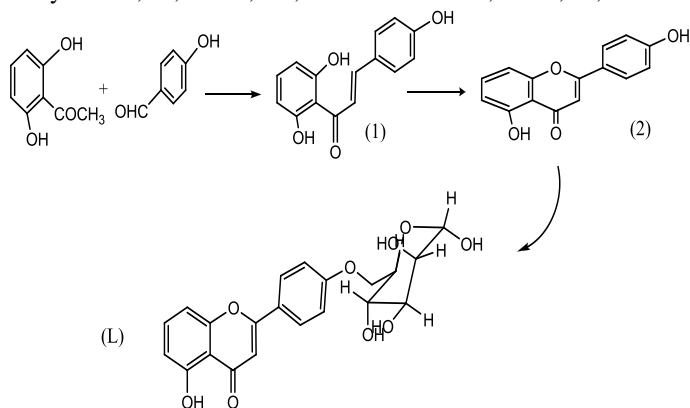
General procedure for the preparation of Flavone – Mannose, 5-hydroxy-2-(4-(((2R,3S,4S,5S,6S)-3,4,5,6-tetrahydroxytetrahydro-2H-pyran-2-yl)methoxy)phenyl)-4H-chromen-4-one (L):

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:

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(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 mmole from L ($\text{C}_{21}\text{H}_{20}\text{O}_9$) 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.

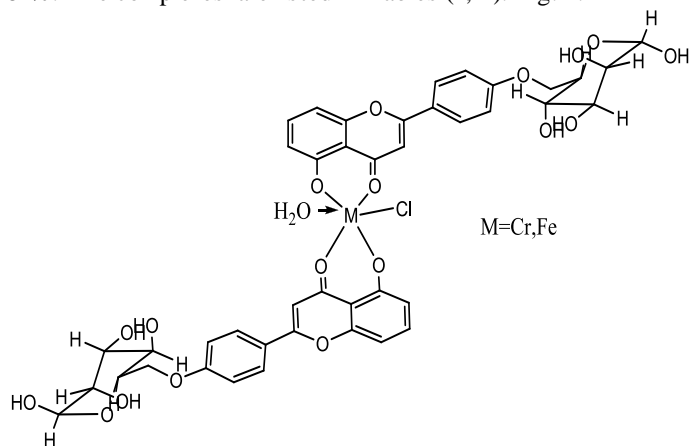


Fig. 1. Suggested structure of the Cr(II) and Fe(III) complexes

Result and Discussion

Claisen Schmidt condensation was chosen for the synthesis of chalcone (1). The reaction partners are 2-hydroxyacetophenone 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 yielded 5-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 Cr(III) or Fe(III) chlorides and 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) performed in ethanolic dimethyl formamide 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 ligand 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^{-1} respectively [17]. However, in the spectra of the complexes there is complete disappearance of peak at 3401 cm^{-1} as 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 515-535 cm^{-1} for complex is assigned to the $\nu(\text{M}-\text{O})$ 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).

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 II, which caused by the transition ($\pi \rightarrow \pi^*$) of the aromatic ring, exhibit absorption maxima at 280 nm. This measured wavelength reflect 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 Ethanol are indicated in Tables (2). These results clearly show values for the molar conductivity of the complexes of bivalent metals are non-electrolyte.

The Molar - Ratio Study

The mole-ratio 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 (Cr(III)) is effected by the absorption due to change in coordinate ion of the ligand complexes as shown in Fig. (3).

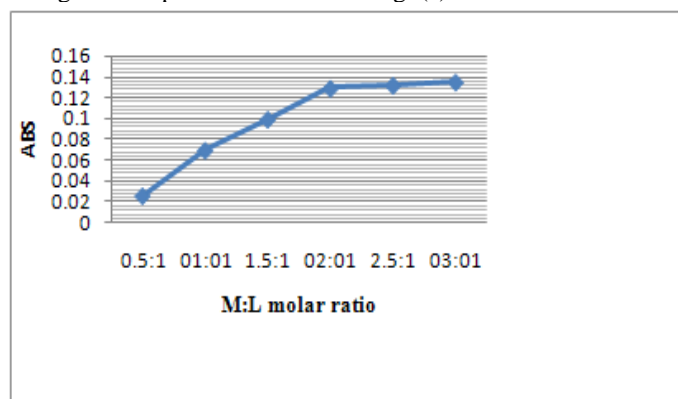


Fig. 3: Plot of the Cr(III) complex formation

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)
[Cr(L) ₂ H ₂ O Cl]	>240	Green	53.88 (53.73)	4.31 (4.21)	5.55 (5.44)
[Fe(L) ₂ H ₂ O Cl]	>240	Brown	53.66 (53.58)	4.29 (4.27)	5.94 (5.93)

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

compound	IR, (cm ⁻¹)			λ_{max} (nm)	assignment	μ_{eff} . BM	* ΔM ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$)
	ν (C=O)	ν (OH)	ν (M-O)				
L	1600(s)	3401 (m)	-	350, 280 250	n $\rightarrow\pi^*$, $\pi \rightarrow\pi^*$	-	-
[Cr(L) ₂ H ₂ O Cl]	1560(s)	3200 (m)	515	261, 298, 380	⁴ A _{2g} \rightarrow ⁴ T _{1g} (P) ⁴ A _{2g} \rightarrow ⁴ T _{1g} (F) ⁴ A _{2g} \rightarrow ⁴ T _{2g}	3.77	6
[Fe(L) ₂ H ₂ O Cl]	1565(s)	3275 (br)	535	265, 310	⁶ A _{1g} \rightarrow ⁴ T _{1g} (P)	5.78	8

br=broad, s=strong, and m=medium , *=molar conductance in 0.001M solutions in DMSO.

Table 3. Structural parameters, bond length (°A) and angles(°) of the [Cr(L)₂H₂O Cl]complex.

Parameters		Parameters	
Bond lengths (°A)		Bond angles(°)	
O(8)-Cr(71)	1.8323	Cr(71)-O(72)-H(102)	120.0002
C(9)-C(10)	1.3510	Cr(71)-O(72)-H(103)	119.9998
O(18)-Cr(71)	1.8200	H(102)-O(72)-H(103)	120.0000
O(19)-C(20)	1.4020	C(38)-O(53)-Cr(71)	113.8682
O(19)-C(22)	1.4020	C(44)-O(43)-Cr(71)	179.9997
O(43)-Cr(71)	1.8200	O(8)-Cr(71)-O(18)	87.0622
C(44)-C(45)	1.3510	O(8)-Cr(71)-O(43)	90.0000
C(45)-C(46)	1.3370	O(8)-Cr(71)-O(53)	111.6037
O(53)-Cr(71)	3.1125	O(8)-Cr(71)-Cl(73)	2.9379
O(54)-C(55)	1.4020	O(8)-Cr(71)-O(72)	118.7194
O(54)-C(57)	1.4020	O(18)-Cr(71)-O(43)	89.9999
Cl(73)-Cr(71)	2.1700	O(18)-Cr(71)-O(53)	45.8620
O(72)-Cr(71)	1.8200	O(18)-Cr(71)-Cl(73)	90.0001
O(72)-H(102)	0.9420	O(18)-Cr(71)-O(72)	131.7248
O(72)-H(103)	0.9420	O(43)-Cr(71)-O(53)	53.6389
Cl(73)-Cr(71)	2.1700	O(43)-Cr(71)-Cl(73)	90.0000
O(72)-Cr(71)	1.8200	O(43)-Cr(71)-O(72)	126.7047
O(72)-H(102)	0.9420	O(53)-Cr(71)-Cl(73)	113.8541
O(72)-H(103)	0.9420	O(53)-Cr(71)-O(72)	129.5736
		Cl(73)-Cr(71)-O(72)	116.5511
		C(9)-C(10)-C(11)	121.8060
		C(9)-C(10)-H(77)	119.0976
		C(11)-C(10)-H(77)	119.0964
		C(9)-O(8)-Cr(71)	103.9460
		C(5)-O(7)-C(11)	111.9999

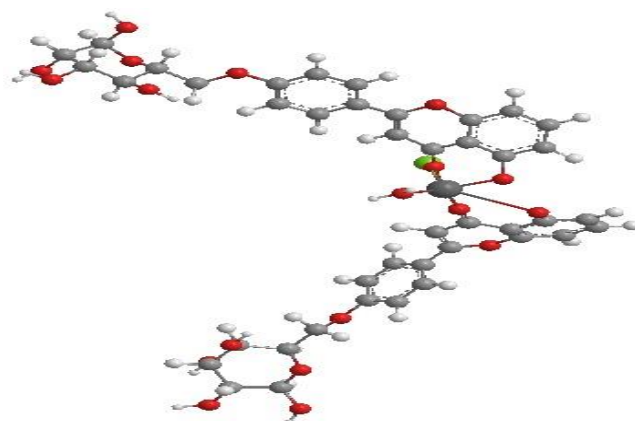
The magnetic moments

The magnetic moments of divalent Chrome and Iron complexes at 3.77 and 5.78 BM ranges respectively at room temperature and are close to the predicted value for tetrahedral geometry around the metal atom [14].

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.(3)

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 Cr(III) 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 [18]. Consequently, the stoichiometry of the complex in methanol solution was investigated using both Jobs method and the slope ratio method [19]. When 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 slope 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 2.01×10^3 and 1.35×10^3 for Cr(III) and Fe(III) complexes, which is in agreement with Irving-Williams [20] order of stability constants of bivalent metal complexes.

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