

In vitro antioxidant activity of new Schiff base ligand and its metal ion complexes

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Abstract:

New Schiff base ligand 2-(((Z)-1-(4-(((E)-4-bromobenzylidene)amino)phenyl) ethylidene)amino)phenol has been synthesized with its metal ion complexes of Mn(II), Fe(III), Co(II), Ni(II) and Cu(II), (C₁, C₂, C₃, C₄ and C₅) metal ions. The synthesized compounds were identified with many techniques such as: FT-IR, UV-visible, ¹H-NMR, ¹³C-NMR, mass spectroscopy, thermal analysis, (CHN) analysis, atomic absorption, magnetic susceptibility and molar conductivity. The complexes have been synthesized by reaction of metal salts with the ligand in (1:2) mole ratio. The ligand was behaved as bidentate ligand attached to the metal ions through N atom of imine group and O atom of 2-amino phenol. The synthesized complexes have been taken the octahedral geometry. Antioxidant study shows that all compounds were exhibited a good antioxidant activity but the copper complex was shown higher activity than other complexes and ligand compared with ascorbic acid as the control.

Key words: Schiff base, antioxidant activity, metal ion complexes, spectrochemical identifications.

1. INTRODUCTION:

The Schiff base is a common name of a class of chemical compounds containing a carbon-nitrogen double bond as a functional group. Schiff base has been known since 1864. The reaction was named refer to German chemist Hugo Schiff who prepared these compounds from simple condensation between an active carbonyl compounds (aldehydes or ketones) with primary amines[1-4]. Schiff bases which are effective as coordinating ligands and widely used in coordinating chemistry because of the relative easiness of preparation, synthetic flexibility and the special property of C=N group, Schiff bases are generally excellent chelating agents, especially when a functional group like -OH or -SH is present close to the azomethine group so as to form a five or six membered ring with the metal ion. Several studies were showed that the presence of a lone pair of electrons in a sp² hybridised orbital of nitrogen atom of the azomethine group is considerable of chemical and biological importance [5, 6]. The most common method for preparing imines is the original reaction discovered by Schiff. Basically it consists in the reaction of an aldehyde (respectively a ketone) with a primary amine and elimination of one water molecule. This reaction can be accelerated by acid catalysis and is generally carried out by refluxing[7]. Schiff bases are described with a high relative stability, Schiff base that derived from aromatic compounds have high stability compared with that derived from aliphatic compounds. Aliphatic ketones react with amines to form imines more slowly than aldehydes; therefore, higher reaction temperatures and longer reaction time are required. Acid catalysts and water removal from the reaction mixture can significantly increase the reaction yields, which can reach 80%–95% values. Aromatic ketones are less reactive than aliphatic ones and require harsh conditions to be converted into imines[8, 9]. Imine group considered as (π- acceptor) this behaviour makes the ligand that including imine group to form stable complexes with metal ions which have a low oxidation state[10]. Compounds derivative from p-amino-

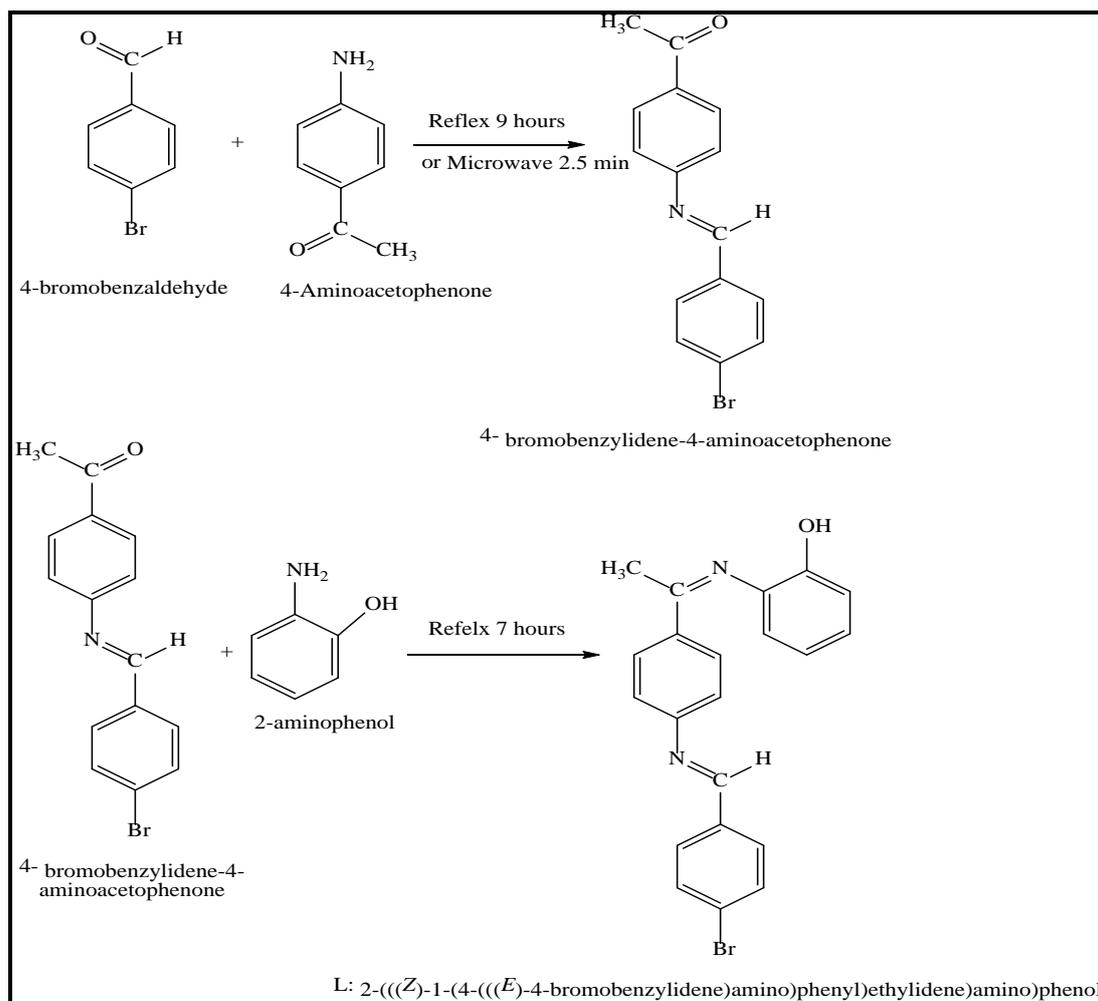
acetophenone are very important chemotherapeutic agent against tumours[11, 12]. Schiff bases and their metal ion complexes have a wide range of application in many fields and the development in the field of bio-inorganic chemistry has increased the interest in Schiff base complexes such as anticancer activity[13], antitumor[14], antioxidant[15, 16], cytotoxicity activity[17, 18], dyes[19] and anti-HIV activity[20].

2. APPARATUS

Fourier transform infrared (FT-IR) spectra were recorded by SHIMADZU 8400s, ultraviolet-visible (UV-Vis) spectra for all the studied compounds have been recorded on the SHIMADZU 1800. ¹H and ¹³C nuclear magnetic resonance (NMR) spectra were measured by a BRUKER AV 400 Avance- III (400 MHz and 100 MHz). The metal content was determined by using (GBC Avanta Ver. 1.33). The atomic absorption analysis was used to determine the metal contents by Nova 350 spectrophotometer. The percentage of carbon, hydrogen and nitrogen (CHN elemental analysis) were carried out by CHN recorded on an EuroEA Elemental Analyzer (EuroEA 3000/Italy). The melting points for all compounds have been carrying out by Gallenkamp melting point apparatus. The molar conductivity for metal ion complexes was carrying out in ethanol (10⁻³ M) which was determined in WTW conduct meter. The magnetic susceptibility of the studied complexes was performed at room temperature by auto magnetic susceptibility balance model Sherwood Scientific. The mass spectra were recorded by using LC-MS (Perkin-Elmer, USA/Flexer SQ 300 M). Thermal analysis of the synthesized complexes and ligand were performed using (SHIMADZU 60-H Thermal Analyser) and Perkin Elmer STA6000thermal analyser.

3. REAGENTS, CHEMICALS AND SUPPLEMENTS

Chemicals and reagents used in this work were of inorganic and bio application grade.



Scheme (1): Synthesis of the ligand

4. THE CHEMICALS (ORGANIC, INORGANIC, AND SOLVENTS)

The chemicals used included 4-bromobenzaldehyde (Sigma-Aldrich), 4-aminoacetophenone (alpha Acer), 2-aminophenol (merch), $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ (Fluka), $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (Fluka), $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (Fluka), $\text{NiCl}_2 \cdot 4\text{H}_2\text{O}$ (Fluka), and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (BDH). The organic solvents which were used included ethanol 95% (BDH), glacial acetic acid (BDH) and Petroleum ether (30–60°C) (Fluka).

5. SYNTHESIS THE LIGAND

The preparation of 4-bromobenzylidene-4-aminoacetophenone was carried out by refluxing an ethanolic solution (25 mL) of 4-aminoacetophenone (1 mmol, 0.135 gm) containing (2-3) drops of glacial acetic acid with an ethanolic solution (25 mL) of 4-bromobenzaldehyde (1 mmol, 0.185 gm) for 7 hrs and then allowed to cool overnight at room temperature. The product was collected, washed thoroughly with ethanol and dried in air. Yield=0.2 gm(70%).

An ethanolic solution of 4-bromobenzylidene-4-aminoacetophenone (25 mL) of the (1 mmol, 0.302 gm) and an ethanolic solution (25 mL) of 2-aminophenol (1 mmol, 0.1 gm) were mixed and refluxed for 7 hrs and allowed to cool over-night at room temperature. The

product was filtered, washed successfully with ethanol and dried in air. Yield=0.33g (83%) as shown in Scheme (1).

6. SYNTHESIS THE COMPLEXES

The complexes had been synthesized by dissolving of (2mmole, 0.787 gm) of the ligand(L) in (15mL) absolute ethanol and mixing with (10 mL, 1mmole) of hot absolute ethanol solution of chloride metals salts of Mn(II), Fe(III), Co(II), Ni(II) and Cu(II) each one of them separately have been added and left them under reflux for 3 hrs and after that allow to cool and added 10mL diethyl ether to precipitate the solid complexes. The crystals were filtered, washed with cold water, ethanol and dried, then recrystallized with ethanol.

7. ANTIOXIDANT ACTIVITY:

Antioxidant activity of (x-substances) has been measured by using stable DPPH radicals with minor adjustments according to Tailor, C. S., et al[21]. (X-substances) for ligand and some of its complexes were used to investigate the scavenging activity. Every sample was mixed with DPPH solution and then completes the quantity to one particular mL using ethanol. Ascorbic acid was used as a positive control. The decline in absorbance was measured

at 517 nm. Scavenging activity measured according to the equation formula below.

$$\text{Scavenging}\% = \frac{\text{Absorbance of control} - \text{Absorbance of sample}}{\text{Absorbance of control}} \times 100\%$$

8. RESULTS AND DISCUSSION:

Physical properties and elemental analysis:

The data of atomic absorption, CHN and chloride analysis as well as the physical properties of the ligand and its metal ion complexes are shown in Table (1). The molecular formulae of the studied compounds were suggested depending on CHN, chloride content, atomic absorption analysis, spectral data and conductivity measurements.

FT-IR spectra of the ligand and its metal ion complexes:

The FT-IR spectrum of the ligand shows broad absorption bands at (2298 to 3463) cm^{-1} weak absorption for phenolic

group, in some complexes the water entered in lattice or coordinated with metal ion and exhibited broad band (3100-3500) cm^{-1} [22]. (C=N) imine group was appeared as sharp band at (1535) cm^{-1} [23, 24], while (C-N) exhibited as a medium band at (1369) cm^{-1} , (C-O) exhibited absorption band at (1245) cm^{-1} [25]. The shift of (C-O) and (C=N) imine in their positions and change the shape or intensity of band compared with the ligand attributable to the coordination of this ligand with the metal ions, and gave an indication that the complexes were formed. (1589) cm^{-1} with a sharp strong intensity attributable to the stretching bands of (C=C) aromatic and (2904) cm^{-1} weak absorption band for H-aliphatic[26]. The range (200-600) cm^{-1} appeared stretching band for (M-O),(M-N)[27] and (M-Cl)[28] in complexes. FT-IR spectral data of the ligand and its complexes were shown in Table (2) and in Figures (1- 6).

Table (1): Physical properties and analytical data for the ligand and its metal ion complexes

symbol	color	m.p °C	Yield %	M.Wt g.mol ⁻¹	Micro Elemental Analysis Found (calc.)			Metal content % Found (calc.)	Chloride content % Found (calc.)
					C%	H%	N%		
L	Yellow	104-108	60	393.28	64.50 (64.13)	4.05 (4.36)	6.90 (7.12)	----	----
C ₁	Light Yellow	202-204	65	948.44	53.57 (53.19)	3.78 (4.04)	5.57 (5.91)	6.12 (5.79)	7.19 (7.48)
C ₂	Green	186-190	75	948.76	33.98 (53.17)	3.87 (3.61)	5.65 (5.91)	5.87 (5.89)	10.88 (11.21)
C ₃	Yellowish-h green	205-208	66	934.24	54.70 (55.05)	3.95 (3.74)	5.81 (6.11)	6.62 (6.43)	7.20 (7.74)
C ₄	Black	225-224	63	957.04	52.69 (52.71)	4.60 (4.00)	5.40 (5.85)	6.89 (6.64)	7.24 (7.41)
C ₅	Yellow	208-210	66	940.86	53.69 (53.62)	3.60 (3.86)	5.40 (5.95)	6.89 (6.95)	7.85 (7.54)

Table (2): FT-IR data of the functional groups of the ligand and its metal ion complexes

Functional group ν cm^{-1}	(O-H), (H ₂ O) ν cm^{-1}	(C-O) ν cm^{-1}	(C=N), (C-N) ν cm^{-1}	(M-N) ν cm^{-1}	(M-O) ν cm^{-1}	(M-Cl) ν cm^{-1}
L	3298-3463	1245	1533, 1369	----	----	----
C ₁	3200-3600	1240	1542, 1379	433.95	345.23	295.09
C ₂	3200-3600	1278	1544, 1344	420	333.66	291.23
C ₃	3200-3600	1240	1544, 1352	433.95	312.45	287.37
C ₄	3200-3600	1240	1546, 1361	435.88	420	300.87
C ₅	3200-3600	1244	1544, 1346	431.31	306.66	273

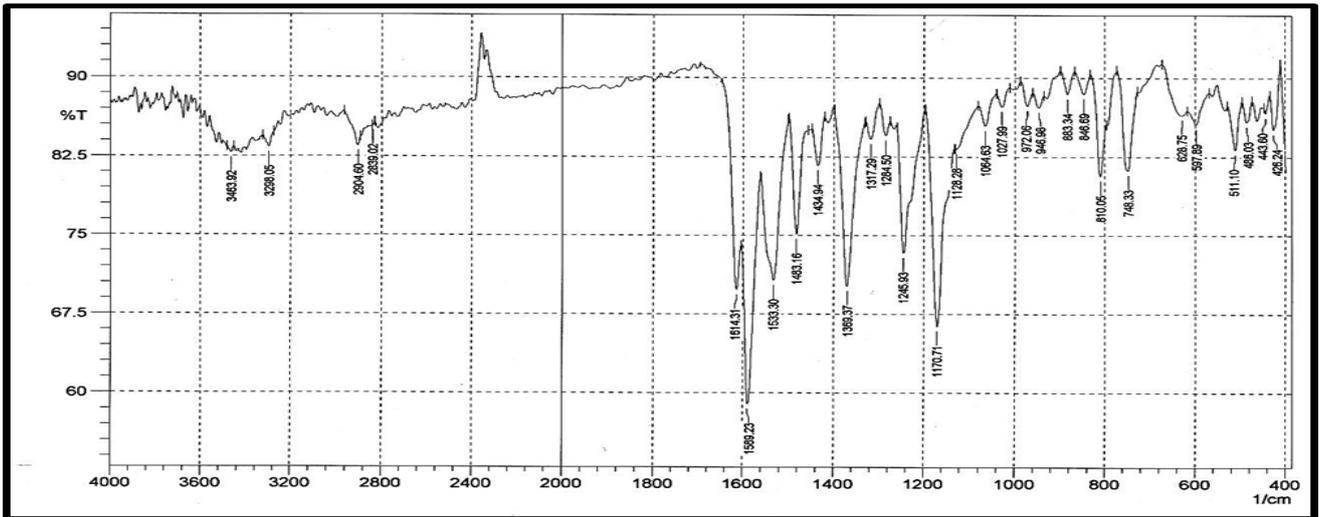


Figure (1): FT-IR spectrum of the ligand

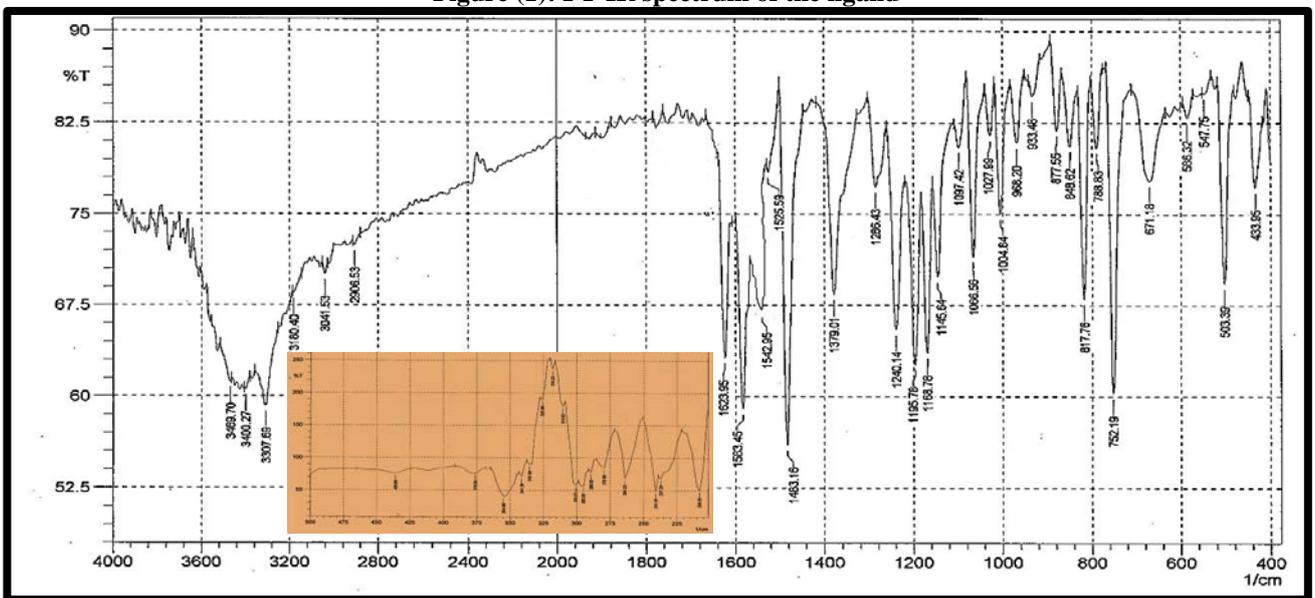


Figure (2): FT-IR spectrum of C₁

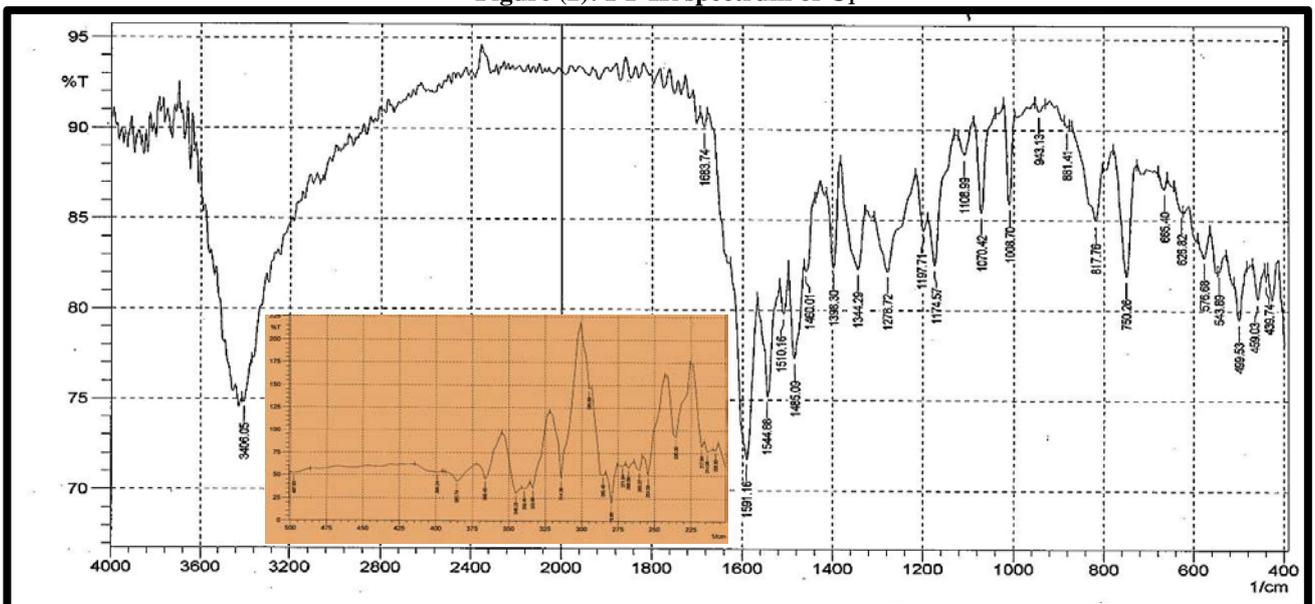


Figure (3): FT-IR spectrum of C₂

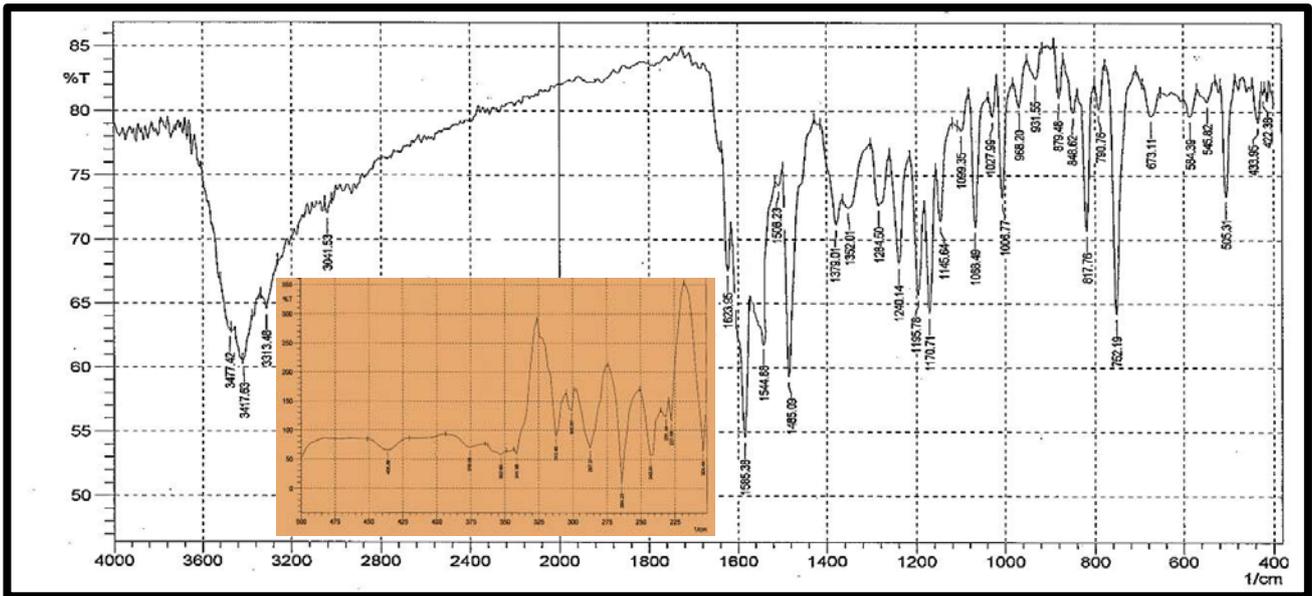


Figure (4): FT-IR spectrum of C₃

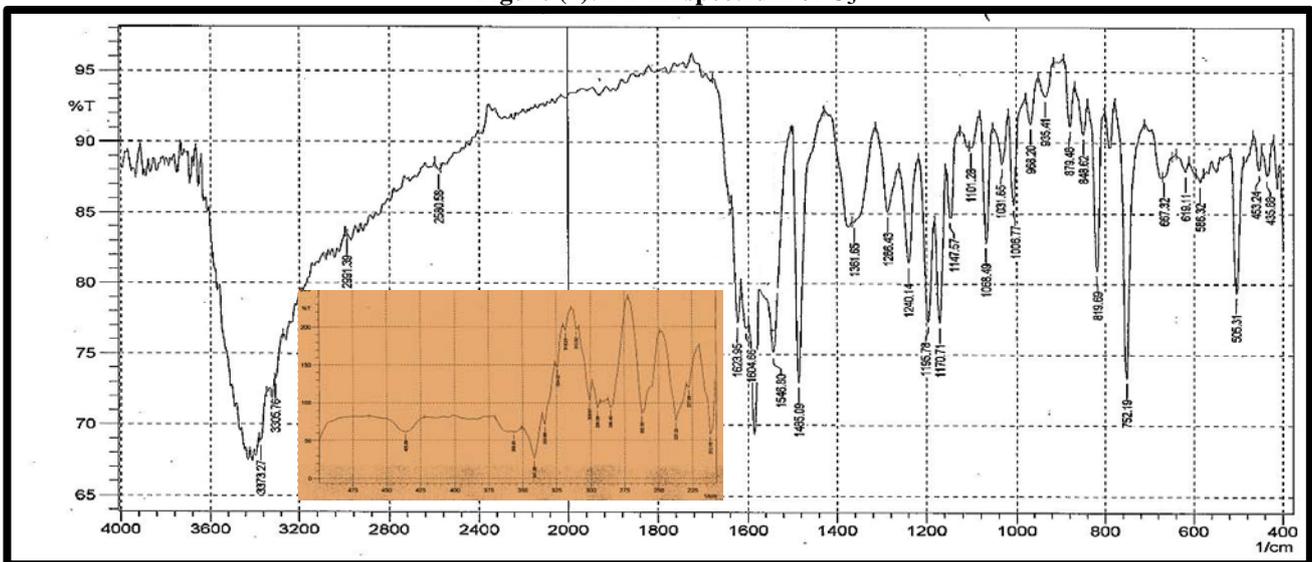


Figure (5): FT-IR spectrum of C₄

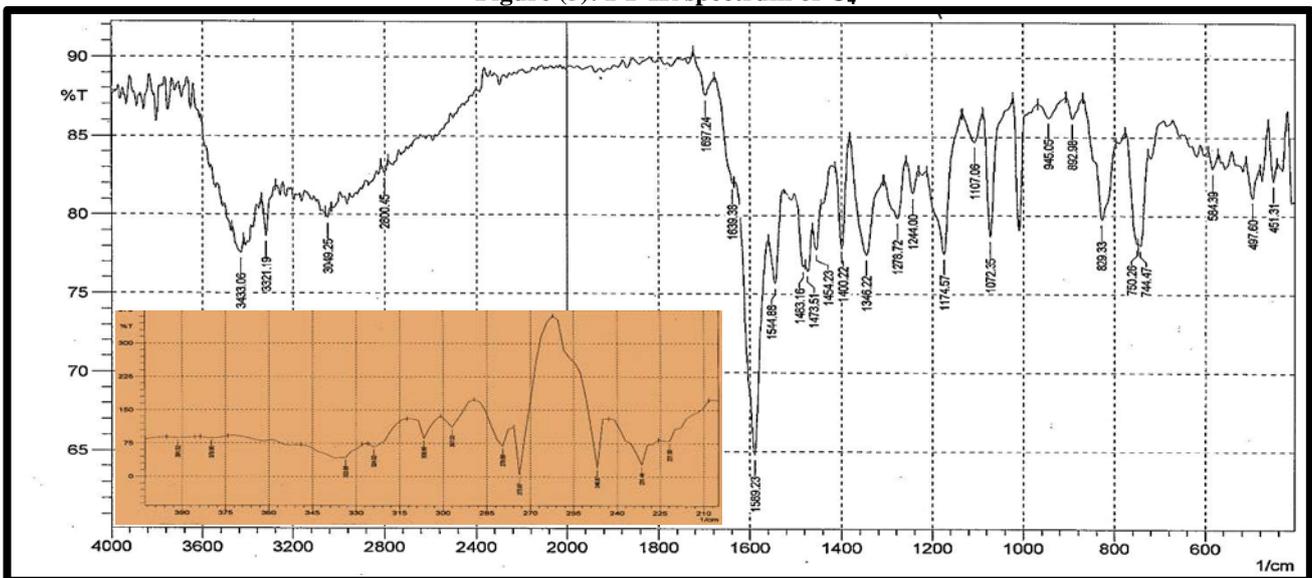


Figure (6): FT-IR spectrum of C₅

¹) due to ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}$ and at (415 nm, 24096 cm^{-1}) for MLCT. (320 nm , 31250 cm^{-1}), (255 nm , 39215 cm^{-1}) bands may be assigned to the transitions of intra ligand charge transfer[46]. The electronic spectrum of the complex(C_4) has been shown two bands observed at (536 nm , 18656 cm^{-1}) due to (${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$) and at (270 nm , 37037 cm^{-1}) band for intra ligand charge transfer[47]. Electronic spectrum of the complex (C_5) exhibited five bands observed at (961 nm , 10405 cm^{-1}) for (${}^2B_{1g} \rightarrow {}^2A_{1g}$), (607 nm , 16474 cm^{-1}) for (${}^2B_{1g} \rightarrow {}^2B_{2g}$) and (502 nm , 19920 cm^{-1}) assigned to (${}^2B_{1g} \rightarrow {}^2E_g$). (438 nm , 22831 cm^{-1}) band for MLCT and (272 nm , 36764 cm^{-1}) absorption band assigned to the intra ligand charge transfer[48, 49].

Thermal analysis of the ligand and its metal ion complexes:

Thermal analysis (TGA and DTA) of the synthesized ligand and its metal complexes have been carried out under nitrogen gas with heating range ($25\text{-}800$) $^{\circ}\text{C}$ and ramp rate of heating ($10^{\circ}\text{C}/\text{min}$). The thermal analysis was performed to expect the suggested structures of the ligand and its complexes. The thermal decomposition data for the ligand and its metal ion complexes were shown in Table (3) and their thermographs were given in Figure (9-13) respectively. The following results were obtained: The first stage which took place at temperature range of ($25\text{-}180$) $^{\circ}\text{C}$ include leaving of water molecules (lattice water) or any lattice molecules such as ethanol in addition of some fragments[50]. The next stages include the decomposition of organic part of the ligand and its complexes may occurs in one or more steps [51]. The final stages involved the residual fragments of the ligand and the metal ion still coordinated to the remaining part of the ligand[52]. The average percentages of fragments were exhibited a good agreement between the calculated and suggested values in addition of compatibility with elemental analyses.

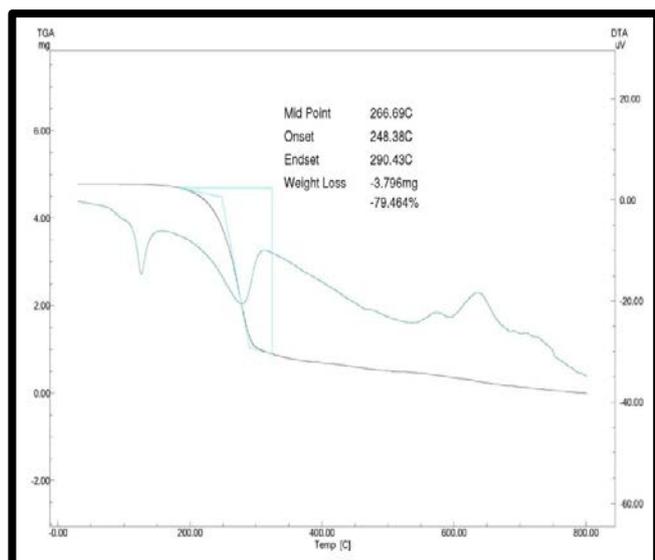


Figure (9): Thermogram of the ligand

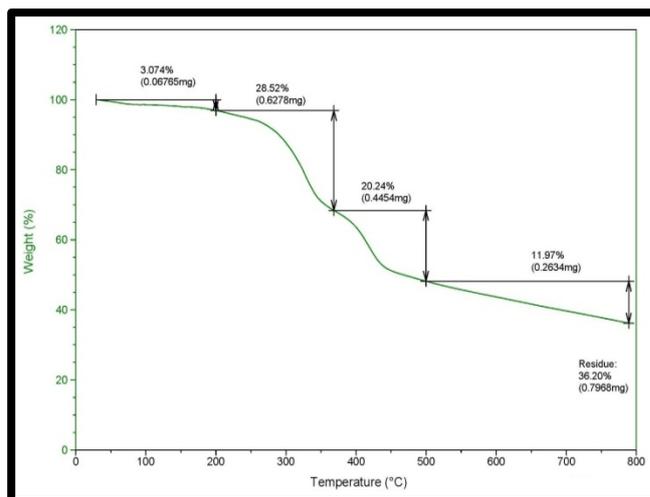


Figure (10): Thermogram of C_1

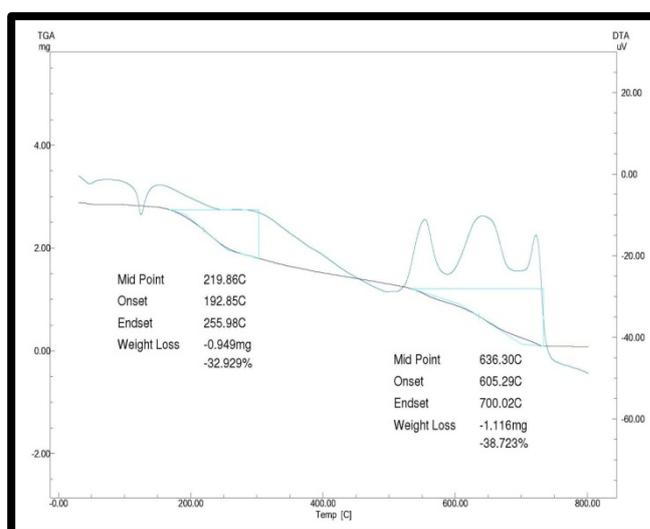


Figure (11): Thermogram of C_3

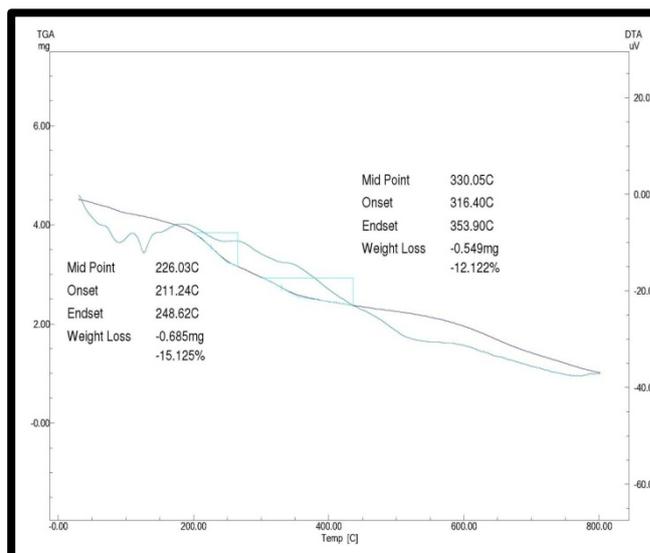


Figure (12): Thermogram of C_4

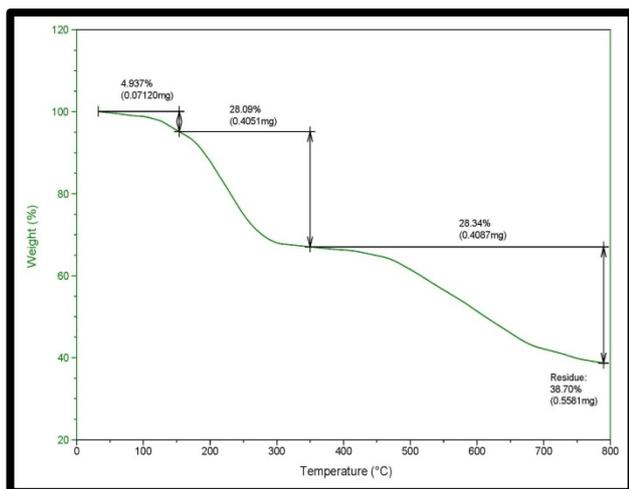


Figure (13): Thermogram of C_5

Mass Spectroscopy:

Mass spectrometry has been used to investigate the molecular ion[53]. The ligand was identify by mass spectrum and compared with suggested molecular weight that obtained from TGA-DTA and CHN techniques and shown a good computability with the mass spectrum and shown a molecular ion at $m/z = 393.39$ as in Figure (14).

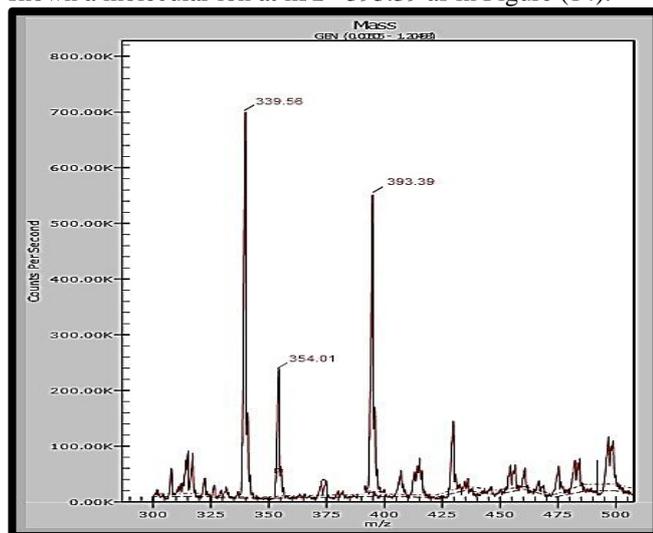


Figure (14): Mass spectrum of the ligand

Molar conductance and magnetic susceptibility mesuerments:

The molar conductance values of the complexes were carried out in ethanol as a solvent at room temperature[54] and the results were given in table (4).The magnetic susceptibility measurements were contributed to determine the suggested structures of complexes. These measurements provided an important information about the ligand field of complexes and also give information about the number of unpaired electrons. The effective magnetic spin of the complexes have been measured by using only a spin magnetic moment[55, 56].

Table (4): Molar conductance values and the values of magnetic moment of the synthesized metal ion complexes

Compound	Molar Cond. $S.cm^2 molL^{-1}$	μ_{eff} (B.M)	
		Cal.	Found
C_1	13.92	5.91	5.02
C_2	39.81	6.92	6.53
C_3	12.2	3.87	3.77
C_4	4.28	2.82	2.97
C_5	3.60	1.73	2.31

The nomenclature and suggested structures of the complexes

The suggested structures of the synthesized complexes have been investigated and confirmed by using infrared (FT-IR), elemental analysis (CHN), UV-Visible spectroscopy, ^1H-NMR , $^{13}C-NMR$ spectroscopy, thermal analysis, mass spectroscopy, molar conductance, atomic absorption and also by magnetic susceptibility measurements. According to the observations obtained the structures of the complexes were suggested as in Figures (15 - 19):

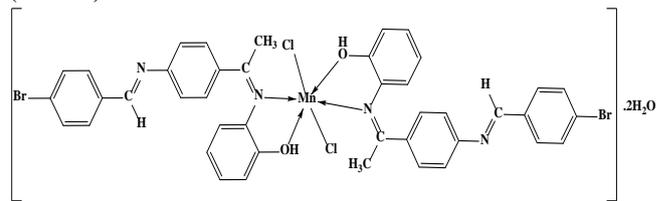


Figure (15) structure and name of C_1 : Didhloro bis (2-(((Z)-1-(4-((E)-4-bromobenzylidene)amino)phenyl)ethylidene) amino)phenol) manganese(II)Dihydrate

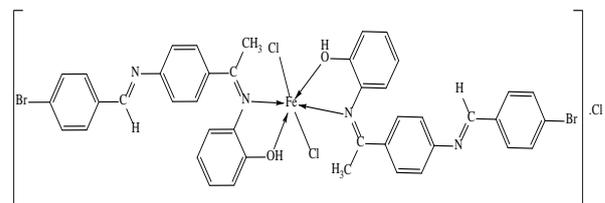


Figure (16) structure and name of C_2 : [Dichloro bis (2-(((Z)-1-(4-((E)-4-bromobenzylidene)amino)phenyl)ethylidene) amino)phenol]iron(III)]Chloride

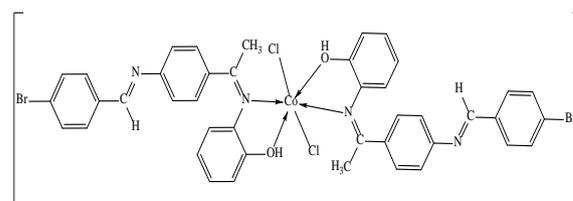


Figure (17) structure and name of C_3 : [Dichloro bis (2-(((Z)-1-(4-((E)-4-bromobenzylidene)amino)phenyl)ethylidene) amino)phenol) cobalt(II)]

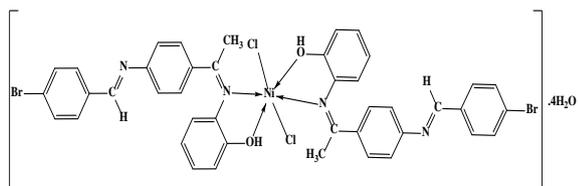


Figure (18) structure and name of C₄: [Dichloro bis(2-(((Z)-1-(4-((E)-4-bromobenzylidene)amino)phenyl)ethylidene)amino)phenol)nickel(II)]Tetrahydrate

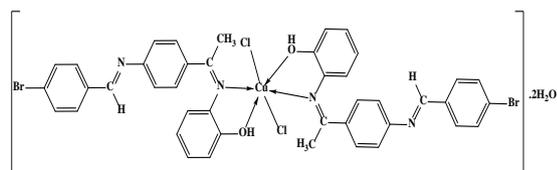


Figure (19) structure and name of C₅: [Dichloro bis(2-(((Z)-1-(4-((E)-4-bromobenzylidene)amino)phenyl)ethylidene)amino)phenol)copper(II)]Dihydrate

Antioxidant activity:

The percentage of scavenging activity of the ligand and its metal ion complexes were studied as shown in Figures (20-25). The antioxidant activity was enhanced significantly after complexation. All the metal ion complexes have been showed comparable or slight less activity to that standard (ascorbic acid). All the metal ion complexes were showed much better activity than the ligand except of (C₄). The copper ion complex was showed a good antioxidant activity than the other metal ion complexes[57].

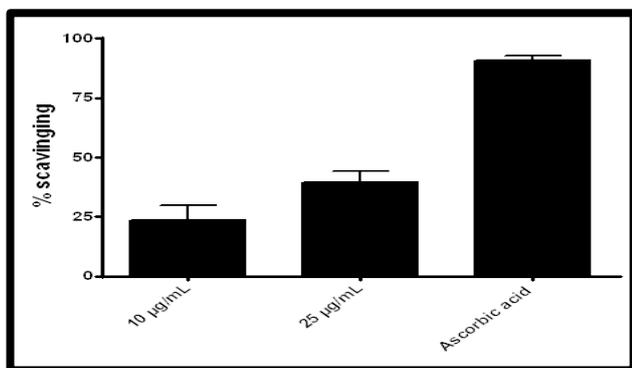


Figure (20): Scavenging activity of the ligand

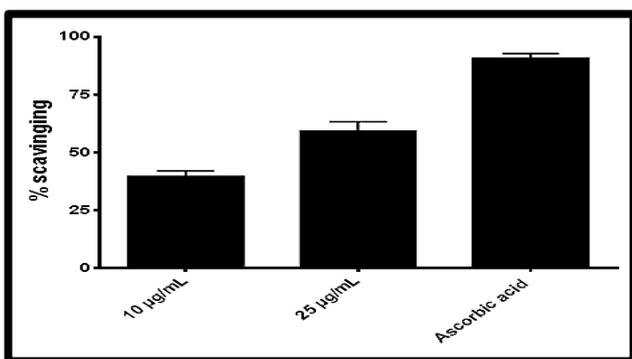


Figure (21): Scavenging activity of C₁

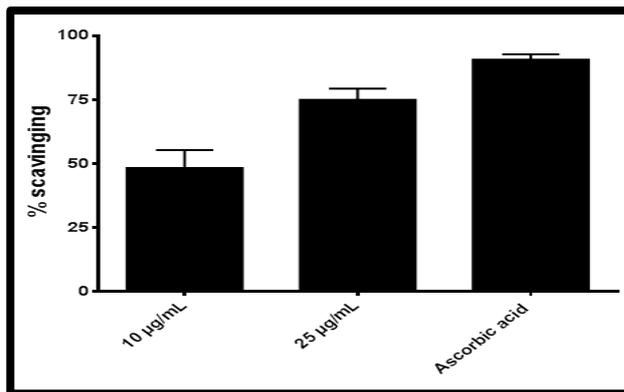


Figure (22): Scavenging activity of C₂

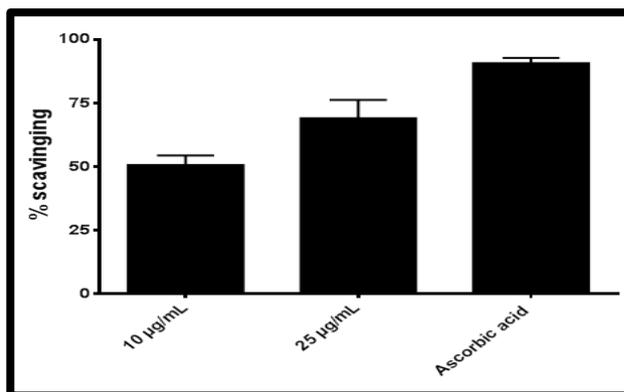


Figure (23): Scavenging activity of C₃

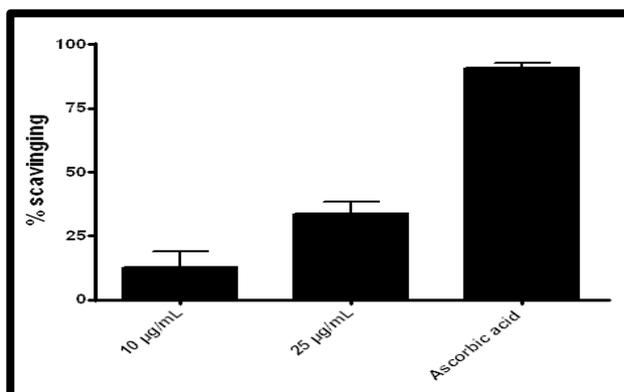


Figure (24): Scavenging activity of C₄

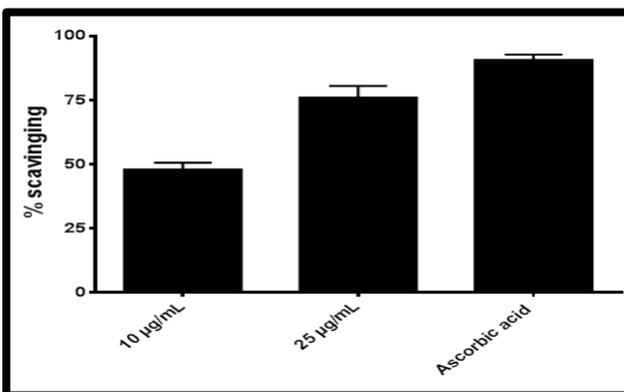


Figure (25): Scavenging activity of C₅

CONCLUSIONS:

New bidentate Schiff base ligand has been synthesized. The ligand has been coordinated to the metal ions through N and O atoms by coordinated bond in mole ratio (1:2) metal: ligand. Spectroscopic, analytical and thermal identifications expected the structures of the complexes were taken the octahedral geometry. According to the molar conductance, the synthesized complexes were non electric except the Fe(III) complex was electric behaves. Cu(II) complex was showing a good antioxidant activity than other complexes and the ligand compared with ascorbic acid as positive control while the Ni(II) complex exhibited lower antioxidant activity than other complexes and the ligand.

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