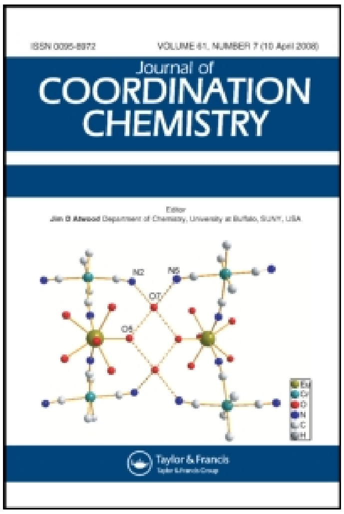


**Journal of Coordination Chemistry**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

# Synthesis, characterization, thermal, and antimicrobial studies of binuclear metal complexes of sulfa-guanidine Schiff bases

Raafat M. Issa[a]; Saleh A. Azim[a]; Abdalla M. Khedr[a]; Doaa F. Draz[a]
[a] Chemistry Department, Faculty of Science, Tanta University, Tanta, Egypt

**To cite this Article** Issa, Raafat M. , Azim, Saleh A. , Khedr, Abdalla M. and Draz, Doaa F.(2009) 'Synthesis, characterization, thermal, and antimicrobial studies of binuclear metal complexes of sulfa-guanidine Schiff bases', Journal of Coordination Chemistry, 62: 11, 1859 — 1870, First published on: 29 July 2010 (iFirst)

**To link to this Article: DOI:** 10.1080/00958970802691432

**URL:** http://dx.doi.org/10.1080/00958970802691432

*Journal of Coordination Chemistry*
Vol. 62, No. 11, 1 June 2009, 1859–1870

# Synthesis, characterization, thermal, and antimicrobial studies of binuclear metal complexes of sulfa-guanidine Schiff bases

RAAFAT M. ISSA, SALEH A. AZIM, ABDALLA M. KHEDR* and DOAA F. DRAZ

Chemistry Department, Faculty of Science, Tanta University, Tanta, Egypt

(*Received 14 July 2008; in final form 4 September 2008*)

A series of metal complexes of Schiff bases derived from condensation of sulfa-guanidine with 1-benzoylacetone ($H_2L^1$), 2-hydroxybenzophenol ($H_2L^2$), dibenzoylmethane ($H_2L^3$), 5-methylisatine ($H_2L^4$), and 1-methylisatine ($H_2L^5$) have been synthesized. The complexes are characterized by elemental analysis, molar conductance, magnetic moment measurements, IR, UV–Vis, $^1$H NMR, and ESR spectra, as well as thermogravimetric analysis. The low molar conductance values indicate the complexes are nonelectrolytes. IR and $^1$H NMR spectra show that $H_2L^1$–$H_2L^5$ are coordinated to metal ions by two bidentate centers. Mn(II), Co(II), Ni(II), and Cu(II) complexes display paramagnetic behavior, whereas the Zn(II)-complex was diamagnetic. All studies confirm the formation of an octahedral geometry for $[Cu_2L^1(AcO)_2(H_2O)_6]\cdot 3H_2O$ (**1**), $[Mn_2L^4(AcO)_2(H_2O)_6]\cdot 2H_2O$ (**6**), $[Ni_2L^4(AcO)_2(H_2O)_6]\cdot 2H_2O$ (**8**), a tetrahedral geometry for $[Cu_2L^2(AcO)_2(H_2O)_2]$ (**2**), $[Cu_2(L^4)_2]$ (**4**), $[Co_2(L^4)_2]\cdot 2H_2O$ (**7**) and $[ZnHL^4(AcO)(H_2O)]\cdot 2H_2O$ (**9**) and a trigonal bipyramid geometry for $[Cu_2L^3(AcO)_2(H_2O)_4]$ (**3**) and $[Cu_2HL^5(AcO)_3(H_2O)_3]\cdot H_2O$ (**5**). $H_2L^4$ was most effective on Gram negative, Gram positive bacteria, and fungi (diameters inhibition zone ranged between 10.5–27.5 mm) after 24 and 48 h, respectively. Complex **8** showed moderate antimicrobial activity. Its minimum inhibitory concentration (MIC) against *Escherichia coli*, *Bacillus subtilis*, *Candida albicans* and *Aspargllus flavas* was 20 mg L$^{-1}$. The compound proved to be of moderate toxicity and its $LD_{50}$ was 20 mg L$^{-1}$.

*Keywords*: Sulfa-guanidine; Schiff bases; Metal complexes

## 1. Introduction

Sulfonamides were the first drugs found to act selectively and could be used systematically as preventive and therapeutic agents against diseases [1]. Sulfur ligands are wide-spread among coordination compounds and are important components of biological transition metal complexes [2]. Metal complexes with sulfur-containing unsaturated ligands are also of great interest in inorganic and organometallic chemistry, especially due to their electrical and magnetic properties [2]. Schiff bases continue to occupy an important position as ligands in metal coordination chemistry [3], almost a century after their discovery. Some metal complexes of the Schiff base derived from [*N*1-(4-methoxy-1,2,5-thiadiazol-3-yl)sulfanilamide] and 2-thiophene carboxaldehyde

---

*Corresponding author. Email: abkhedr2001@yahoo.com

*Journal of Coordination Chemistry*
ISSN 0095-8972 print/ISSN 1029-0389 online © 2009 Taylor & Francis
DOI: 10.1080/00958970802691432

were synthesized and subjected to spectroscopic and thermal studies [4]. Organotin(IV) complexes of biologically active Schiff bases derived from condensation of 2-acetylfuran and 2-acetyl-thiophene with sulfa-guanidine, sulphathiazole, sulphisoxazole, and sulphadiazine were prepared [3]. Oxovanadium(IV) complexes with pyrazolone-based sulfa drug Schiff bases of bioinorganic and medicinal relevance were studied [5]. Recently, metal complexes of four new azo compounds derived from sulfa drugs have been investigated [6]. Metal complexes containing two or more metal ions per molecule find wide application in biological systems, catalysis, and material science [7–9], beside their peculiar spectroscopic and magnetic properties [10–12].

Hence, it is imperative to look into structure and biological activity of binuclear transition metal complexes of Schiff bases derived from sulfa-guanidine and 1-benzoylaceto ($H_2L^1$), 2-hydroxybenzophenol ($H_2L^2$), dibenzoylmethane ($H_2L^3$), 5-methylisatine ($H_2L^4$), and 1-methylisatine ($H_2L^5$), which have not been reported. The aim of the present study is to synthesize Mn(II), Co(II), Ni(II), Cu(II), and Zn(II) complexes of such Schiff bases (especially binuclear ones), characterize the complexes by spectral and analytical methods as well as study their activities against gram negative (*Escherichia coli*) and gram positive (*Bacillus subtilis*) bacteria and fungi (*Candida albicans* and *Aspargllus flavas*).

## 2. Experimental

### 2.1. *Reagents*

All chemicals used in the present work were of analytical reagent grade (AR). The solvents used were either spectroscopic pure from BDH or purified by the recommended method [13].

### 2.2. *Physical measurements*

Elemental microanalyses of the prepared compounds for C, H, and N were performed at the micro-analytical unit of Tanta University using a Perkin–Elmer 2400. The melting points were measured using a Gallenkamp instrument. The molar conductance of the complexes in DMF ($1 \times 10^{-4}$ M solution) was performed at 25°C using a conductance bridge of the type 523 conductometer. The infrared spectra were recorded on a Perkin–Elmer 1430 IR spectrophotometer within the range 4000–200 $\mathrm{cm}^{-1}$ as KBr discs. The $^1$H NMR spectra were carried out using a Varian Mercury Oxford NMR 300 Hz spectrometer after dissolving the samples in DMSO-d6 using tetramethylsilane as internal standard. The electronic absorption spectra were recorded using a Shimadzu UV–Vis 160A spectrophotometer with a rectangular quartz cell of dimensions $0.2 \times 1$ cm from 200 to 900 nm. The magnetic susceptibilities of the solid complexes were recorded at room temperature by Gouy's method using a magnetic susceptibility instrument (20 Kilo Gauss). Mol susceptibilities were corrected for diamagnetism of the component atoms applying Pascal's constants. The thermal gravimetric analysis (TGA) was carried out in a dynamic nitrogen atmosphere (20 $\mathrm{ml\,min}^{-1}$) with a heating rate of 10°C $\mathrm{min}^{-1}$ using a Shimadzu TG-50 thermogravimetric analyzer. Room temperature x-band powder electron spin resonance spectra of the complexes were recorded using a

Jeol spectrometer model JES-FE2XG Jeol equipped with an E101 microwave bridge. The magnetic field was calibrated with dipicrylhydrazyl. Metal contents were determined complexometrically using standard EDTA titration [14].

### 2.3. *Preparation of ligands*

Five Schiff bases ($H_2L^1$–$H_2L^5$) were prepared by condensation of methanolic solution (40 mL) of sulfa-guanidine (10 mmol, 2.14 g) with 1-benzoylacetone (10 mmol, 1.62 g), dibenzoylmethane (20 mmol, 4.49 g), 5-methylisatine (20 mmol, 3.22 g), 2-hydroxy-benzophenol (10 mmol, 1.98 g), and 1-methylisatine (20 mmol, 3.22 g) in methanol on a water bath for 8 h according to the recommended method [15]. The condensation products $H_2L^1$–$H_2L^5$ separated on cooling, were filtered off and purified by repeated recrystallization from appropriate solvent (yield 75–80%).

### 2.4. *Synthesis of Mn(II), Co(II), Ni(II), Cu(II), and Zn(II) complexes*

A stirred solution of the ligands $H_2L^1$ (5 mmol, 1.79 g), $H_2L^2$ (5 mmol, 3.13 g), $H_2L^3$ (10 m mol, 2.55 g), $H_2L^4$ (5 mmol, 1.97 g) or $H_2L^5$ (5 m mol, 2.55 g) in methanol (50 mL) were mixed with a methanolic solution (40 mL) of $(CH_3CO_2)_2Cu \cdot H_2O$ (10 mmol, 2.00 g) for preparation of Cu(II) complexes **1**–**5**, respectively. Also, $HL^4$ solution (10 mmol, 1.98 g) was mixed with $(CH_3CO_2)_2Mn \cdot 2H_2O$ (10 mmol, 2.68 g), $(CH_3CO_2)_2Co \cdot 4H_2O$ (10 mmol, 1.99 g), $(CH_3CO_2)_2Ni \cdot 4H_2O$ (10 mmol, 2.49 g), or $(CH_3CO_2)_2Zn \cdot 2H_2O$ (10 mmol, 2.20 g) for preparation of complexes **6**–**9**. The reaction mixture was refluxed for about 3 h; the solution was then evaporated to 1/3 volume and cooled to 0°C. The solid complexes separated, were filtered, washed with methanol and dried in vacuum over anhydrous calcium chloride.

### 2.5. *Antimicrobial activity*

Test microorganisms, Gram negative bacteria (*E. coli NRRL-B-3704*), Gram positive bacteria (*B. subtilus NRRL-B-4378*) and fungi (*C. albicans ATCC 10231* and *A. flavus NRRL 6554*), were obtained from the Department of Botany and Microbiology, Faculty of Science, Tanta University. The experiment determined the minimal inhibitory concentrations (MIC) of the antagonistic substance against the test organism by agar dilution method. The media used were nutrient broth medium for bacteria and Sabouraud's medium for fungi. Each culture medium was enriched with different concentrations of Ni-$L^4$, 8. The concentrations were 5, 10, and 20 mg $L^{-1}$. The results were recorded after 24 h for bacteria and 48 h for fungi. The number of living colonies or colony forming units (CFU) $mL^{-1}$ was counted using the bioassay method [16].

### 2.6. *Cytotoxicity test*

Brine shrimp Artemia have been used previously in bioassay systems, but Meyer *et al.* [17] developed a method for the determination of the lethal dose for pure compounds. In this study, 8 was tested at initial concentrations of 5, 10 and 20 mg $L^{-1}$ in vials containing 5 ml of sea water and ten Brine Shrimp Artemia in each of three replicates. Survival animals were counted after 24 h.

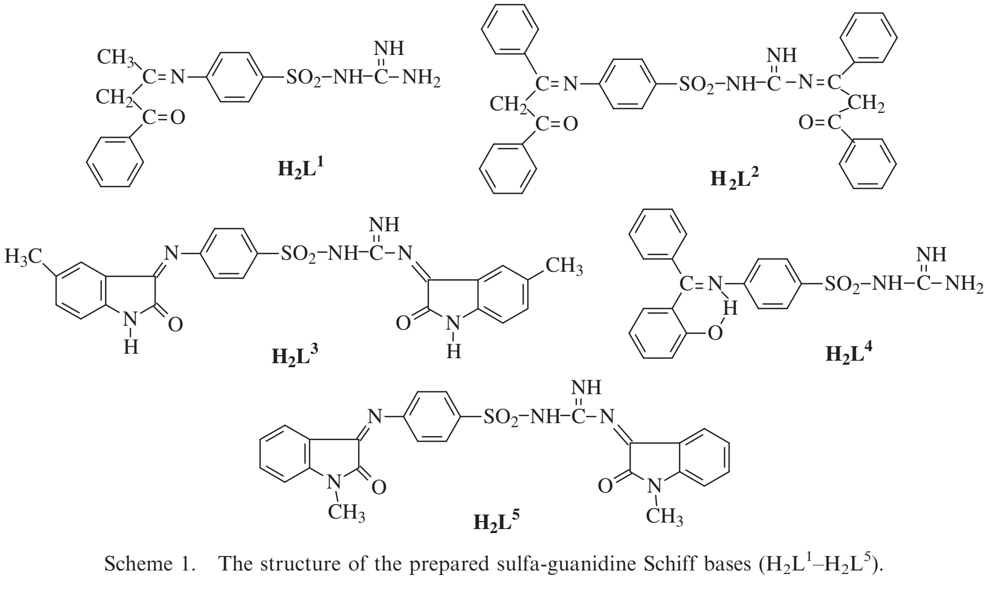
## 3. Results and discussion

Sulfa-guanidine Schiff bases $H_2L^1$–$H_2L^5$ (scheme 1) were purified by recrystallization several times from the appropriate solvent until constant melting point. Their purity was confirmed by elemental analysis which agrees with the suggested molecular formula [18].

### 3.1. *Elemental analysis and molar conductance of the prepared complexes*

The analytical data of the prepared complexes (table 1) show that the calculated and found values of C, H, and N are in satisfactory agreement supporting the suggested molecular formula listed. The results reveal that the 2 : 2 Cu(II) complex (**4**) and Co(II) complex (**7**), derived from $H_2L^4$, have no acetate. All other complexes contain one acetate for each metal. The second acetate was librated in the reaction medium as acetic acid during preparation of the complexes. The proton displaced would be that of an $OH^-$ formed through enolization of the bonding center [19]. The metal contents were determined by the recommended methods of analysis [14]. The reaction takes place between $H_2L^1$, $H_2L^2$, $H_2L^3$, and $H_2L^5$ with Cu(II) in ratio 2 : 1 (M : L) for **1**, **2**, **3**, and **5**, respectively, and 2 : 2 (M : L) for **4** and **7** for $H_2L^4$ with Cu(II) and Co(II). Complexes **6** and **8** for $H_2L^4$ with Mn(II) and Ni(II) have a ratio 2 : 1 (M : L), whereas Zn(II) has a ratio 1 : 1 (M : L) with $H_2L^4$ in **9**.

The complexes are soluble in DMSO and DMF and sparingly soluble in ethanol and methanol. The molar conductance values (table 1) reveal that the complexes are



Scheme 1. The structure of the prepared sulfa-guanidine Schiff bases ($H_2L^1$–$H_2L^5$).

Table 1. Elemental analysis and physical properties of the prepared solid complexes.

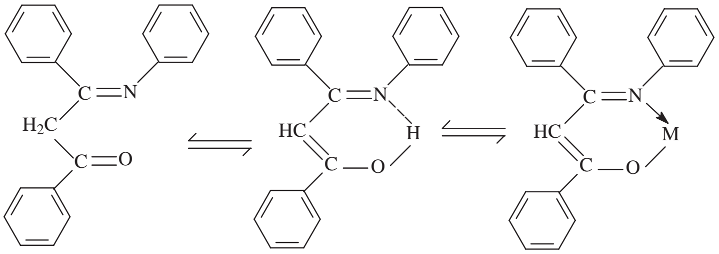
| Comp. no. | Molecular formula (Empirical formula) | Color (M. Wt) | m.p. (°C) (Ωm) | Elemental analysis | | | |
|---|---|---|---|---|---|---|---|
| | | | | Calcd % (found) | | | |
| | | | | %C | %H | %N | %M |
| **1** | $[Cu_2L^1(AcO)_2(H_2O)_6] \cdot 3H_2O$ ($C_{21}H_{40}Cu_2N_4SO_{16}$) | Green (763.73) | 248–250 (3.6) | 33.03 (33.49) | 5.28 (4.66) | 7.34 (7.32) | 16.64 (16.31) |
| **2** | $[Cu_2L^2(AcO)_2(H_2O)_2]$ ($C_{41}H_{38}Cu_2N_4SO_{10}$) | Faint orange (905.94) | 153–155 (5.1) | 54.36 (54.11) | 4.23 (3.96) | 6.18 (6.01) | 14.03 (14.16) |
| **3** | $[Cu_2L^3(AcO)_2(H_2O)_4]$ ($C_{29}H_{32}Cu_2N_6SO_{12}$) | Brown (815.77) | 286–288 (5.7) | 42.70 (42.78) | 3.95 (3.89) | 10.30 (10.69) | 15.58 (16.03) |
| **4** | $[Cu_2(L^4)_2]$ ($C_{40}H_{32}Cu_2N_8S_2O_6$) | Olive green (911.98) | 288–290 (5.8) | 52.68 (52.63) | 3.54 (4.01) | 12.29 (12.61) | 13.94 (13.61) |
| **5** | $[Cu_2HL^5(AcO)_3(H_2O)_3] \cdot H_2O$ ($C_{31}H_{35}Cu_2N_6SO_{14}$) | Orange (874.81) | 238–240 (4.3) | 42.56 (43.02) | 4.03 (3.45) | 9.61 (9.19) | 14.53 (14.22) |
| **6** | $[Mn_2L^4(AcO)_2(H_2O)_6] \cdot 2H_2O$ ($C_{24}H_{38}Mn_2N_4SO_{15}$) | Brown (764.52) | 288–290 (9.5) | 37.71 (37.24) | 5.10 (4.80) | 7.33 (7.14) | 14.37 (14.38) |
| **7** | $[Co_2(L^4)_2] \cdot 2H_2O$ ($C_{40}H_{36}Co_2N_8S_2O_8$) | Brown (938.76) | 286–288 (3.9) | 51.18 (50.76) | 3.87 (3.76) | 11.94 (11.69) | 12.56 (12.87) |
| **8** | $[Ni_2L^4(AcO)_2(H_2O)_6] \cdot 2H_2O$ ($C_{24}H_{38}Ni_2N_4SO_{15}$) | Green (772.03) | 298–300 (6.3) | 37.34 (37.71) | 4.96 (4.66) | 7.26 (7.74) | 15.20 (14.82) |
| **9** | $[ZnHL^4(AcO)H_2O] \cdot 2H_2O$ ($C_{22}H_{26}N_4SO_8Zn$) | Buff (571.93) | 278–280 (4.0) | 46.62 (46.08) | 4.58 (4.57) | 9.80 (9.81) | 11.43 (11.02) |

non-electrolytes in DMF [20], hence the acetate anions, when present, will be inside the coordination sphere.

### 3.2. *Infrared absorption spectra of the prepared $H_2L^1$–$H_2L^5$ complexes*

Previous studies on metal chelates of Schiff bases of sulfa-drugs [19] indicated that metal ions are bonded to the ligand either through the Schiff base or the sulphonamide part for mononuclear complexes, while for binuclear ones both centers contribute. On examining the infrared spectra of the metal chelates in comparison to the corresponding free ligands [18], the following observations can be made (table 2).

1. IR spectra of all complexes showed broad bands at 3458–3381 $cm^{-1}$, which can be assigned to $\nu$(OH) of water associated with complexes. The presence of coordinated water renders it difficult to confirm the enolization of the OH groups on complex formation [21] from the stretching vibration.
2. Absorption bands for the free ligands at 1609–1519 and 3339–3216 $cm^{-1}$ due to $\nu$(C=O) and $\nu$(NH), respectively, show obvious shifts in the spectra of **1**–**9** indicating participation of these groups in complex formation. Compound **4** which is free from $H_2O$ is an exception, where the stretching vibration of OH disappeared confirming the formation of M–O bond.
3. Spectra of all complexes show a shift in the position of C=N bands to higher frequencies due to coordination of the azomethine nitrogen to the metal in chelate formation [22].
4. The $SO_2$ group modes of the $H_2L^{1-5}$ ligands appeared as sharp bands at 1306–1364 and 1138–1178 $cm^{-1}$ ($\nu_{asym}SO_2$) and ($\nu_{sym}SO_2$), respectively, slightly shifted to higher or lower frequencies upon coordination to the transition metals [23, 24]. The shift of the $SO_2$ stretching vibration frequencies may be attributed to transformation of the sulfonamide ($SO_2NH$) to the enol form (SO(OH)N) as a result of complex formation to give a more stable six-membered ring [23, 24].
5. From these observations and the previous studies [19, 21, 25], complex formation takes place through proton displacement of the free OH or from an enolic OH formed through a keto-enol tautomerism in the coordination centers of the molecule as follows:



Or

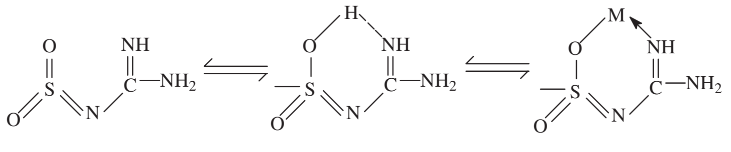


Table 2. Assignment of the IR spectral bands ($cm^{-1}$) of the complexes under study.

| Comp. no. | $\nu$(OH) and/or $\nu(H_2O)$ | $\nu$ ($NH_2$) | $\nu$ (NH) | $\nu$ (C=O) | $\nu$ (C=N) | $\nu$ (M–O) | $\nu$ (M–N) | $\nu$ ($SO_2N$) | $\nu$ (S=O) | $\nu$ (C–S) |
|---|---|---|---|---|---|---|---|---|---|---|
| **1** | 3424 | 3340 | 2925 | 1622 | 1531 | 554 | 419 | 1307 1178 | 1234 | 686 |
| **2** | 3422 | – | 3057 | 1601 | 1536 | 539 | 412 | 1336 1146 | 1237 | 650 |
| **3** | 3427 | – | 3210 | 1621 | 1535 | 555 | 449 | 1319 1139 | 1267 | 688 |
| **4** | – | 3316 | 3062 | 1595 | 1534 | 580 | 460 | 1306 1187 | 1236 | 697 |
| **5** | 3429 | – | 3205 | 1606 | 1540 | 559 | 400 | 1366 1175 | 1242 | 688 |
| **6** | 3428 | 3346 | 3218 | 1555 | 1555 | 556 | 411 | 1339 1132 | 1243 | 664 |
| **7** | 3458 | 3350 | 3059 | 1593 | 1534 | 558 | 458 | 1307 1181 | 1230 | 696 |
| **8** | 3430 | 3373 | 3220 | 1630 | 1530 | 555 | 445 | 1343 1168 | 1244 | 686 |
| **9** | 3429 | 3330 | 3216 | 1623 | 1535 | 545 | 400 | 1336 1174 | 1243 | 694 |

This is supported by the appearance of two new bands within the ranges 583–519 and 460–345 $cm^{-1}$ due to $\nu$(M–O) and $\nu$(M–N) [26], respectively. The assignment of bands of diagnostic importance in the IR spectra of all complexes under study is collected in table 2.

### 3.3. $^1H$ *NMR spectra for Zn(II) complex (9)*

The $^1H$ NMR spectrum of complex **9** is compared with that of $H_2L^4$ [20] in order to determine the center of chelation and replaceable hydrogen on complex formation. The OH group at 10.40 ppm disappeared indicating the displacement of its hydrogen through complex formation [27]. The $^1H$ NMR spectrum of Zn(II)-complex displayed two new signals at 1.81 and 2.50 ppm for water and for $CH_3$ from acetate, respectively. Signals appearing at 7.36–7.69, 6.50 and 5.64 due to $\delta_{Ar}$, $\delta_{NH}$, $\delta_{NH_2}$ in the free ligand shifted to 7.33–7.83, 6.58, and 5.83 on complex formation. The downfield shift of these signals is due to deshielding by Zn(II) [28].

### 3.4. *Electronic spectra*

Electronic absorption spectra of the complexes under investigation were recorded from 12,500 to 50,000 $cm^{-1}$ using nujol mull and DMF solution. The Cu(II)-complex (**1**) showed two bands in nujol mull at 28,571, 16,667 and in DMF at 222,222, 14,286 $cm^{-1}$ which can be assigned to $^2B_{1g}$–$^2B_{2g}$ and $^2E_{2g}$–$2B_{2g}$ electronic transitions in an octahedral configuration. The Cu(II)-complexes (**2**) and (**4**) gave two bands in nujol mull at 25,000, 20,000 $cm^{-1}$ for **2** and 26,316, 18,181 $cm^{-1}$ for **4** and in DMF at 26,316, 20,000 $cm^{-1}$ for **2** and 25,000, 20,000 $cm^{-1}$ for **4**, assigned to $^2T_2$–$^2E$ in tetrahedral geometry. Spectra in Nujol mull showed bands at 20,000, 16,667 $cm^{-1}$ for **3** and 23,256, 15,152 $cm^{-1}$ for **5** and in DMF showed bands at 20,833, 16,667 $cm^{-1}$ for **3**, and 22,222, 14,286 $cm^{-1}$ for **5**, assigned to transitions corresponding to trigonal bipyramidal structure ($D_3h$) with ground state $dz^2$ which sometimes exhibits a shoulder in the near IR-region [29, 30]. The Mn(II)-complex (**6**) displayed two bands at 20,000, 16,667 and 20,000, 16,667 $cm^{-1}$ in nujol mull and DMF, respectively, assigned to $^6A_{1g}$–$^4T_{2g}$ and $^6A_{1g}$–$^4E_g$ transitions in an octahedral geometry [31, 32]. The Co(II)-complex (**7**) gave two bands in nujol mull at 26,316, 22,222 $cm^{-1}$ and in DMF showed bands at 23,256, 20,833 $cm^{-1}$ assigned to $^4T_1(F)$–$^4T_2(F)$ and $^4T_1(F)$–$^4T_1(P)$ transitions indicating tetrahedral geometry [33]. The binuclear Ni(II)-complex (**8**) showed two bands in nujol mull at 25,641, 23,258 $cm^{-1}$ and in DMF at 25,000, 16,667 $cm^{-1}$ assigned to $^3A_{2g}$–$^3T_{1g}(F)$, $^3A_{1g}$–$^3T_{1g}(P)$ transitions in octahedral structure [34]. The electronic spectra of the Zn(II)-complex (**9**) in nujol mull and DMF displayed mainly CT bands at 29,412, 20,833 $cm^{-1}$ and 22,222, 16,667 $cm^{-1}$ which can be assigned as metal to ligand or ligand to metal charge transfer transitions.

### 3.5. *Magnetic susceptibility studies*

Magnetic susceptibilities of the prepared metal complexes were determined at room temperature by the Gouy method. The observed magnetic moments of Cu(II) complexes were 1.919, 1.776, 1.366, 1.845, and 1.726 for **1**–**5**, respectively. These values lie around the theoretical spin only value 1.72 BM, which means that one unpaired electron is present [35]. Taking into account the elemental analyses, **1** has octahedral geometry while **2** and **4** are tetrahedral. Complexes **3** and **5** are trigonal bipyramid. It would be difficult to arrive at the structure of Mn(II) complex from the magnetic moment value, as Mn(II) ion in various geometries would exhibit the spin only value around 5.9 BM. The $\mu_{eff}$ of **6** = 5.6 BM indicates five unpaired electrons in high-spin arrangement. The observed magnetic moment of **7** was 3.984 BM, showing the presence of three unpaired electrons in tetrahedral geometry [36]. The Ni(II) complex (**8**) shows magnetic moment of 3.063, which reveals the presence of two unpaired electrons in an octahedral geometry [37]. The Zn(II) complex (**8**) is diamagnetic as expected.

### 3.6. *ESR spectra*

The powder X-band ESR spectra of **1**, **2** and **6** have been recorded at room temperature. The calculated $g_{eff}$, $g_{\|}$ and $g_{\perp}$ are 1.6180, 2.0120, 1.5570 and 2.019, 2.3600, 1.8150 for **1** and **2**, respectively. The $g_{eff}$ value and the shape of the ESR spectra for the binuclear Cu(II)-complex (**1**) indicate octahedral geometry, whereas **2** has a tetrahedral geometry. The $g_{eff}$ values of **1** are obviously different from that of **2**. From the observed *g*-values of the Cu(II)-complexes it is clear that $g_{\|} > g_{\perp}$, indicating that the unpaired electron is predominantly in the $d_{x^2-y^2}$ orbital [38] giving $^2B_{1g}$ as the ground state. The calculated $g_{eff}$, $g_{\|}$, and $g_{\perp}$ values for **6** are 1.8970, 2.1760, and 1.7870. The negative deviation of $g_{eff}$ value from the value of the free electron ($g_{eff} = 2.0023$) may be attributed to covalent character of the bond between the Mn(II) ion and the ligand. The spectra of the complex showed a broad signal which indicates non-equivalent environment with octahedral geometry around Mn(II), and a measurable covalent character in the bonding between the ligand and metal ion [39].

### 3.7. *Thermogravimetric analysis and kinetic parameters for each decomposition step*

The TGA curves of **1**–**5** were recorded from ambient temperature up to 800°C under $N_2$ gas flow at a heating rate of 10°C $min^{-1}$. The stages of decomposition, temperature range as well as found and the calculated mass loss percentages are collected in

Supplemental Material (see online). It is clear that the thermal decomposition of the metal complexes under interest occurs in five essential steps; the evaporation of lattice water molecules, elimination of coordinated water molecules, removal of the acetate anion, and finally decomposition of the organic ligand which can take place in two steps with the formation of copper oxide as a final product.

### 3.8. *Antimicrobial activity*

To look at the therapeutic promise of the investigated ligands and complexes, all were checked for antibacterial activity against gram negative (*E. coli*) and gram positive (*B. subtilis*) bacteria as well as fungi (*C. albicans* and *A. flavas*). The test organisms can achieve resistance to antibiotics through biochemical and morphological action. The capability of the prepared ligands ($H_2L^1$, $H_2L^2$, $H_2L^3$, $H_2L^4$, and $H_2L^5$) to inhibit the growth of microorganism was tested on solid media through diameter of inhibition zone, which depends on the active group in the ligands and the tested organism. $H_2L^4$ was the most effective on Gram negative, Gram positive bacteria, and fungi (diameters inhibition zone ranged between 10.5–27.5 mm) after 24 and 48 h, respectively. The capability of complexes of $H_2L^4$ with Mn(II), Co(II), Ni(II), Cu(II), and Zn(II) to inhibit growth of the tested microorganism on solid media is shown in table 3. The $HL^4$-Ni(II) complex (**8**) showed the highest antimicrobial activities on Gram negative,

Table 3. Diameters of inhibition zones (mm) produced by 0.005 gm solid of $HL^4$-complexes against different organisms.

| | | | Complexes | | |
|---|---|---|---|---|---|
| Organism | 6(Mn) | 7(Co) | 8(Ni) | 4(Cu) | 9(Zn) |
| *E. coli* | 25 | N.D. | 30 | N.D. | 35.5 |
| *B. subtilis* | −ve | −ve | 40 | −ve | −ve |
| *C. albicans* | 15 | −ve | 30.5 | −ve | 29.5 |
| *A. flavas* | 1.5 | −ve | 27.5 | −ve | 2.5 |

N.D. = Not detected under the experimental condition.

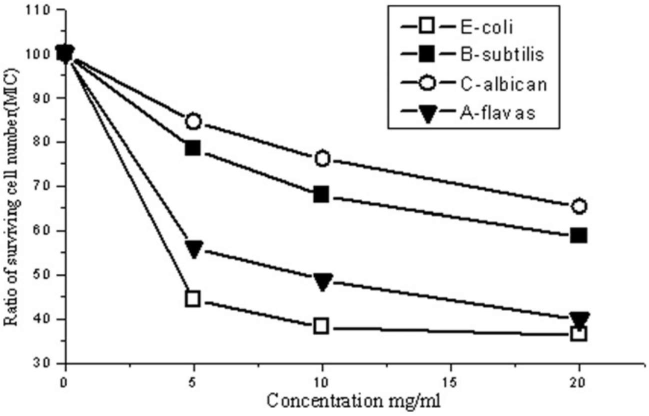
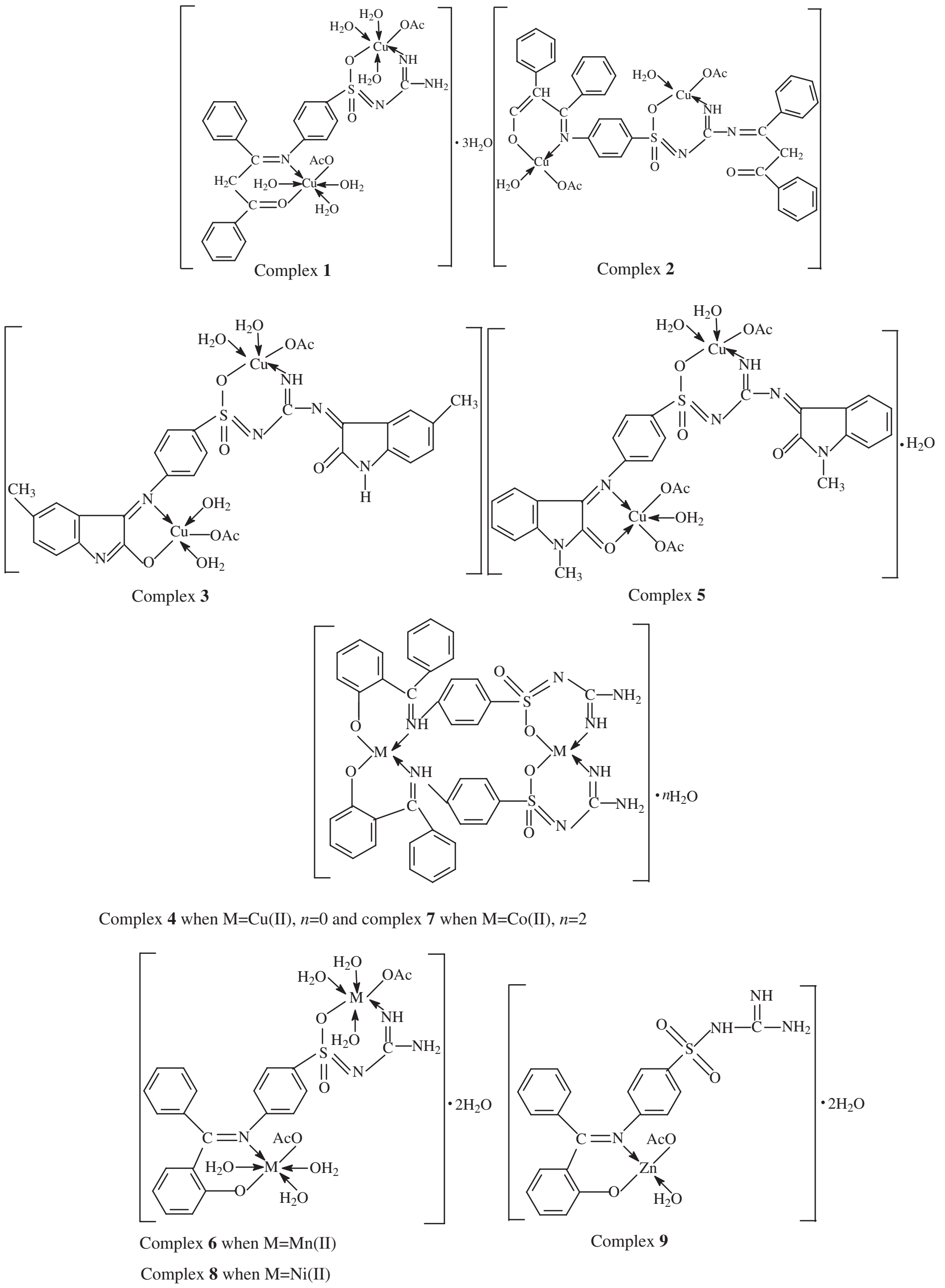


Figure 1. Growth inhibitions of different concentrations of **8** with *E. coli*, *B. subtilis*, *C. albican* and *A. flavas*.



Complex **1**

Complex **2**

Complex **3**

Complex **5**

Complex **4** when M=Cu(II), *n*=0 and complex **7** when M=Co(II), *n*=2

Complex **6** when M=Mn(II)

Complex **8** when M=Ni(II)

Complex **9**

Scheme 2. Representative structures of **1**–**9**.

Gram positive and fungi (inhibition zone diameters range between 27.5 and 40 mm) after 24 and 48 h.

### 3.8.1. Minimum inhibitory concentrations (MIC).

The MIC of **8** was determined using four test organisms. Different concentrations of the pure antagonistic material were added to nutrient broth (for the test bacteria) and to Sabouraud's medium (for the test fungi). Rodriguez *et al.* [40] stated that cobalt and nickel complexes inhibited the growth of bacteria and fungi. The growth inhibitory effect of 8 differed among the bacteria and fungi, stronger in the order *E. coli* > *A. Flavas* > *B. subtilis* > *C. albicans*. The colony forming unit of the test organisms decreased by increasing the complex concentration (figure 1).

**3.8.2. Cytotoxicity test.** The cytotoxicity of **8** was determined using Artemia; a positive correlation exists between Artemia death and human carcinoma cytotoxicity. Brine shrimp is used in many pre-screens for potential antitumor activity. The results clearly show that 50% of lethal dose was $20\,\mathrm{mg\,L^{-1}}$ where the number of living Artemia decreased by 50% compared to control (100%). Increasing the complex concentration leads to mortality of all Artemia. Addition of concentration ($40\,\mathrm{mg\,L^{-1}}$) decreased the living Artemia to 10% compared to untreated. The toxicity of **8** was also studied to determine the degree of safety of this complex. The results indicate that the tested complex has moderate effect as evidenced by its $LD_{50}$ ($20\,\mathrm{mg\,L^{-1}}$) against brine shrimp. Similar results were obtained by a series of structurally related 1H-pyrazol derivatives [41]. The mode of action of **8** is interpreted in terms of the following sequence of elementary processes [42–44], adsorption into bacterial cell surface, diffusion through the cell wall, binding to cytoplasmic membrane, disruption of the cytoplasmic membrane, release of cytoplasmic constituents such as $K^+$ and $Na^+$ ions, DNA, RNA and death of the cell. Complex **8** showed higher antimicrobial activities and overcame some defense mechanisms. The organism could be resistant to transition metal complexes due to extrachromosomal (DNA or plasmids) [45]. Plasmids often encode special proteins which inactivate toxic metal ions by modifying the site of inhibition, changing the permeability of cell membranes and creating special efflux mechanisms. The metal complexes show more biological activity than their ligands due to the synergistic effect of both ligand and metal ion. Also, the low molecular weight allows easier permeability of the Zn(II) complex compared with the Cu(II) complexes. The easier permeability of the Zn(II) complex affords higher activity toward the microbe cells.

## 4. Conclusion

Based on spectroscopic and analytical data, structures of the complexes formed between $H_2L^1$, $H_2L^2$, $H_2L^3$ and $H_2L^5$ and Cu(II) and $H_2L^4$ metal complexes are represented in scheme 2.

## References

[1] P. Nagpal, R.V. Singh. *Appl. Organomet. Chem.*, **18**, 221 (2004).

[2] C.Y. Wu, L.H. Chen, W.S. Hwang, H.S. Chen, C.H. Hung. *J. Organomet. Chem.*, **689**, 2192 (2004).

[3] H.L. Singh, S. Varshney, A.K. Varshney. *Appl. Organomet. Chem.*, **13**, 637 (1999).

[4] C.M. Sharaby. *Spectrochim. Acta, Part A*, **66**, 1271 (2007).

[5] R.C. Maurya, S. Rajput. *J. Mol. Struct.*, **794**, 24 (2006).

[6] G.G. Mohamed, A.M. Mohamed, A.M. Gad-Elkareem. *Spectrochim. Acta, Part A*, **68**, 1382 (2007).
[7] X. Chen, X. Peng, J. Wang, Y. Wang, S. Wu, L. Zhang, T. Wu, Y. Wu. *Euro. J. Inorg. Chem.*, **34**, 5400 (2007).
[8] H. Ngyen, M. Orlamuender, D. Pretzel, I. Agricola, U. Sternberg, S. Reissmann. *Pept. Sci.*, **14**, 1010 (2008).
[9] S. Albedyhl, M.T. Averbuch-Pouchot, C. Belle, B. Krebs, J.L. Pierre, E. Saint-Aman, S. Torelli. *Euro. J. Inorg. Chem.*, **6**, 1457 (2001).
[10] J. Du, X. Meng, X. Zeng. *Chin. J. Chem.*, **26**, 421 (2008).
[11] R.M. Issa, A.M. Khedr, A. Tawfik. *Synth. React. Inorg. Met.-Org. Chem.*, **34**, 1087 (2004).
[12] T.M. Ismail, A.M. Khedr, S.M. Abu-El-Wafa, R.M. Issa. *Coord. Chem.*, **57**, 1179 (2004).
[13] D.D. Perrin, W.L.F. Armarego, D.R. Perrin. *Purification of Laboratory Chemicals*, Pergamon Press, Oxford (1980).
[14] A.I. Vogel. *A Text Book of Quantitative Inorganic Analysis*, Longmans, London (1969).
[15] H.D. Saw. *J. Am. Chem. Soc.*, **101**, 154 (1967).
[16] T.J. Franklin, G.A. Snow. *Biochemistry of Antimicrobial Action*, 4th Edn, Chapman and Hall, London (1989).
[17] B.N. Meyer, N.R. Ferrigni, J.E. Putnam, L.B. Jacobsen, D.E. Nichols, J.L. Mclughlin. *Planta Med.*, **45**, 31 (1982).
[18] R.M. Issa, S.A. Atyia, A.M. Khedr, D.F. Draz. (in course of publication) c. f. D.F. Draz, MSc thesis, *Studies of Dianiles of Sulfa-guanidine with some Hydroxylketons and Their Metal Complexes*, Chemistry Department, Faculty of Science, Tanta University (2007).
[19] K.Y. El-Baradie, M. Gaber. *Chem. Pap.*, **57**, 317 (2003).
[20] W.J. Geary. *Coord. Chem. Rev.*, **7**, 81 (1971).
[21] G.G. Mohameda, M.A.M. Gad-Elkareem. *Spectrochim. Acta, Part A*, **68**, 1382 (2007).
[22] R.K. Agarwal, H. Agarwal. *Synth. React. Inorg. Met.-Org. Chem.*, **26**, 1163 (1996).
[23] G.G. Mohamed, C.M. Sharaby. *Spectrochim. Acta, Part A*, **66**, 949 (2007).
[24] C.M. Sharaby, G.G. Mohamed, M.M. Omar. *Spectrochim. Acta, Part A*, **66**, 935 (2007).
[25] K.Y. El-Baradie. *Monatsh. Chem.*, **136**, 1139 (2005).
[26] K. Nakamoto. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 4th Edn, John Wiley and Sons Inc., New York (1986).
[27] J. Knoeck, J.A. Buchholz. *Talanta*, **18**, 895 (1971).
[28] A.B.P. Lever. *Inorganic Electronic Spectroscopy*, 2nd Edn, Elsevier, Amsterdam (1984).
[29] B.J. Hathway, D.E. Billing. *J. Coord. Chem. Rev.*, **5**, 14 (1970).
[30] I.M. Procter, B.J. Hathway, P. Hedesson. *J. Inorg. Nucl. Chem.*, **34**, 369 (1972).
[31] D. Nicholls. *Complexes of the First Row Transition Elements*, Macmillan Chemistry Text, London (1978).
[32] U. Agarwal, G. Saxena. *Egypt. J. Chem.*, **28**, 8 (1985).
[33] M.G.B. Drew, F.S. Esho, A. Lavery, S.M. Nelson. *J. Chem. Soc., Dalton Trans.*, **1**, 545 (1984).
[34] F.A. Cotton, G. Wilkinson. *Advanced Inorganic Chemistry*, Interscience Publishers, London (1974).
[35] L. Sacconi. *Coord. Chem. Rev.*, **1**, 126 (1966).
[36] N.T. Madhu, P.K. Radhakrishnan. *Trans. Met. Chem.*, **25**, 287 (2000).
[37] N.S. Gill, R.S. Nyholm. *J. Chem. Soc.*, 3997 (1959).
[38] P.K. Dhara, S. Pramanik, T. Lu, M.G.B. Drew, P. Challopadhyay. *Polyhedron*, **23**, 2457 (2004).
[39] I. Fidone, K.W.H. Stevens. *Proc. Phys. Soc.* (London), **37**, 116 (1957).
[40] M.C. Rodriguez-Argüelles, E.C. Lopez-Silva, J. Sanmartin, A. Bacchi, C. Pelizzi, F. Zani. *Inorg. Chim. Acta*, **357**, 2543 (2004).
[41] A.A. Bekhit, T. Abdel-Azeem. *J. Bioorg. Med. Chem.*, **12**, 1935 (2004).
[42] W.B. Hungo, A.R. Longwoth. *J. Pharm. Pharmcol.*, **16**, 655 (1964).
[43] W.B. Hungo, A.R. Longwoth. *J. Pharm. Pharmcol.*, **18**, 569 (1966).
[44] A. Kanazawa, T. Ikeda, T. Endo. *J. Polym. Sci.*, **31A**, 1441 (1993).
[45] L.G. Leduc, G.D. Ferroni. *FEMS Microbiol. Rev.*, **14**, 103 (1994).