Preparation and Characterization of Cu (II), Mn(II) and Zn(II)complexes with new sulfamethoxazole Compounds

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Abstract:

Acetophenone sulfamethoxazole and 3-Nitrobenzophenone sulfamethoxazole were prepared from the reaction of sulfamethoxazole with two ketones. The prepared ligands were identified by (C.H.N) analysis and UV-VIS, FT-IR spectroscopic techniques. Metal complexes of the two ligands were prepared in an aqueous alcohol with Zn (II) Mn (II) and Cu (II) ions with a molar ratio1:1. The proposed general formula for the resulting complexes was [MLCl₂.H₂O]H₂O .The complexes were characterized by (C.H.N) technique , spectroscopic methods ,conductivity, atomic absorption ,magnetic susceptibility measurements and melting point. According to the results obtained, the suggested geometry is to be octahedral for all the complexes.

Key words: Sulfamethoxazole, Schiff base complexes, Metal complexes, Antibacterial.

Introduction:

Sulfonamides are structural analogs and competitive antagonists of para-amino benzoic acid (PABA). Sulfamethoxazole derivatives are widely used in the medicine and pharmaceutical industry because of their extensive biological effectiveness [1]. Sulfamethoxazole prevents the formation of dihydrofolic acid, a compound which makes the bacteria able to survive. It has been reacted with selected ketons and aldehydes to give Schiff bases [2].Schiff bases play an important role in the coordination chemistry and are used as chelating agents with transition elements [3]. Schiff base metal complexes have a wide interest in clinical, biological and analytical applications [4].They show biological activities including anti bacterial, anti fungal, anti cancer and herbicidal activities, anti-tubercular activities [5]. Moreover, some metal complexes of these ligands have been found to promote rapid healing of burns in humans and animals [6]. The current study investigated the preparation and properties of some metal ion complexes with sulfamethoxazole derivatives.

Materials and Methods:

All the chemicals used in this work are of high purity. The electronic spectra were measured on (Shimadzu UV -160 A) Ultra Violet-Visible Spectrophotometer. The infrared spectra were measured using (Shimadzu FTIR-
8600 S) Fourier Transform Infrared, Spectrophotometer (4000-400) cm⁻¹ with samples prepared as KBr discs. Metal analysis was determined by using (A.A-680) Shimadzu atomic absorption spectrophotometer. The conductivity measurements were obtained using conduct meter WTW; the complexes were dissolved in DMF, element microanalyses were recorded by microanalysis (C.H.N) in Al-Albaite University in Jordan, the magnetic susceptibility values of the prepared complexes were obtained by using magnetic susceptibility balance Johnosn Matthey. The melting points of the prepared ligands and the complexes were measured by using melting point apparatus Gallenkamp M.F.B-60.

Synthesis of Schiff bases (L1, L2)

Schiff bases L1 and L2 were prepared from reaction of sulfamethoxazol (0.01mole) with two different ketones (aceto phenone and 4-nitro benzo phenone) (0.01mole in 25 ml absolute ethanol and drops of glacial acetic acid). The mixture was heated under reflux for 5 hrs. Precipitates were flittered and recrystallized from ethanol. The synthesis route is shown in Scheme (1).

![Scheme 1: Synthesis of Schiff bases (L1, L2).](image)

Preparation of Metal Complexes

An aqueous solution containing 0.17g, 0.136g and 0.197g (1mmole) of CuCl₂.2H₂O, ZnCl₂ and MnCl₂.4H₂O respectively was added gradually with stirring to ethanolic solution (1mmole) of the ligand (L1). The reaction mixture was heated under reflux for 3 hours, keeping the reaction mixture over night to give solid products and recrystallization from ethanol. The complexes of L2 were prepared by the same method.
Results and Discussion:
The ligands were prepared by condensation reaction between sulfamethoxazol with two different ketones. All prepared complexes were colored, soluble in organic solvent such as EtOH, DMSO and DMF and stable toward air. (Table 1) includes some physical properties and elemental analysis, of prepared ligands and their complexes.

Table (1):- Elemental Analysis and Physical Properties of the Ligands and the Complexes.

| Compounds         | Color       | Yield% | M.P °C | Elemental microanalysis | found. (Calc)% |
|-------------------|-------------|--------|--------|-------------------------|---------------|
|                   |             |        |        | M% | C% | H% | N% | %S |
| L1                | Yellow      | 85     | 136    | -  | 52 | (51.2) | 3.64 | (3.80) | 10.44 | (10.1) | 10.75 | (6.92) |
| [Zn L1Cl2(H2O)2]  | Dark yellow | 62     | 178    | 10.7| 44.63| (44.23) | 2.96 | (2.88) | 8.3 | (8.82) | 6.25 |
| [Cu L1Cl2(H2O)2]  | Dark green  | 50     | 172    | 9.4 | 42.57| (43.63) | 2.31 | (2.84) | 8.15 | (8.85) | 6.8 |
| [Mn L1Cl2(H2O)2]  | Cream       | 54     | 230    | 7.1 | 44.11| (44.23) | 3.00 | (2.88) | 8.00 | (8.97) | 6.57 |
| L2                | Cream       | 70     | 170    | -  | 49.86| (49.23) | 4.30 | (4.78) | 16 | (16.77) | 12.31 |
| [Zn L2Cl2(H2O)2]  | Dark yellow | 78     | 180    | 12.23| 41.00| (40.95) | 3.64 | (3.22) | 9.27 | (9.83) | 8.21 |
| [Cu L2Cl2(H2O)2]  | Green       | 55.5   | 172    | 14 | 40 | (41) | 3.76 | (3.23) | 6.85 | (7.99) | 7.98 |
| [Mn L2Cl2(H2O)2]  | Light yellow | 57    | 146    | 10.09| 34.40| (34.21) | 3.28 | (3.20) | 11.3 | (11) | 8.31 |

The Infrared Spectral Studies:
FT-IR spectrum of compound (L1) showed absorption bands at 1593 cm⁻¹, 3387 cm⁻¹, 1161-1327 cm⁻¹, 2839-2989 cm⁻¹, 3089 cm⁻¹, 1373 cm⁻¹ and 1685 cm⁻¹ assigned to ν(C=N) in heterocyclic, ν(N-H), ν(SO₂), ν(C-H) aliphatic, ν(C-H) aromatic, ν(C-NO₂) and ν(C=N) azomethine of the Schiff base respectively as shown in Table (2)[7].

Comparing the IR spectra of the complexes and free ligands, the following differences were observed:
I. A strong band at (3387) cm⁻¹ in the ligands assigned to (NH) group was shifted to lower frequency on chelating with metal ion indicating the (NH) group acting as a coordinating site [8].
II. The shift of two sulfonamide vibrations (symmetric as well as the
asymmetric one) toward lower shift number in the spectra of the complexes as compared to the spectra of corresponding ligands (Table 2). Further support (M-O) bonding [9].

III. The strong band at 1597 and 1593 cm⁻¹ assigned to (C=N) in heterocyclic ring exhibit lower shift as support (M-N) bonding.

IV. The metal complexes show a broad band in the region (3466-3475) cm⁻¹ and a new band at 829-833 cm⁻¹ that assigned to the (O-H) stretching vibration and out of plane bending of water molecules coordinated to the complexes [10].

V. The new bands observed at (416-570) cm⁻¹ are tentatively assigned to ν (M-N) and (M-O) (Metal-Ligand) [11, 12].

VI. The appearance of a band at (1685, 1620) cm⁻¹ in the ligands assigned to ν(C=N) azomethine, this band remains almost at the same position in the complexes and hence suggests that the azomethine nitrogen is not taking part in coordination [7].

### Table (2): FT-IR Bands of Ligands and Metal Complexes

| Comp. | ν(OH) | ν(C=N) cyclic | ν(C=N) azomethine | ν(C-N) | ν(N-H) | ν(SO₂) | ν(M-O) | ν(M-N) |
|-------|-------|---------------|-------------------|--------|--------|--------|--------|--------|
| L1    | -     | 1593          | 1685              | 1504   | 3387   | 1161   | 1327   | -      |
| [Zn L₁Cl₂(H₂O)]H₂O | 3475 | 1597          | 1616              | 1473   | 3213   | 1157   | 1319   | 509    | 447    |
| [Cu L₁Cl₂(H₂O)]H₂O | 3474 | 1593          | 1620              | 1473   | 3387   | 1134   | 1323   | 524    | 474    |
| [Mn L₁Cl₂(H₂O)]H₂O | 3474 | 1593          | 1620              | 1469   | 3213   | 1138   | 1315   | 570    | 442    |
| L2    | -     | 1597          | 1620              | 1504   | 3379   | 1157   | 1365   | -      |
| [Zn L₂Cl₂(H₂O)]H₂O | 3465 | 1597          | 1616              | 1473   | 3213   | 1091   | 1315   | 505    | 474    |
| [Cu L₂Cl₂(H₂O)]H₂O | 3464 | 1597          | 1616              | 1400   | 3303   | 1114   | 1319   | 574    | 416    |
| [Mn L₂Cl₂(H₂O)]H₂O | 3466 | 1597          | 1615              | 1469   | 3298   | 1311   | 543    | 420    |

**The Electronic Spectral Studies**

The free ligand solution display high intensity peaks in the UV regions at 248 and 311 nm, which are assigned to (π→π*) electronic transitions for functional groups, C=N and S=O respectively [13]. The absorption band appeared at (291 nm) which can be attributed to (π→π*) transition for the aromatic system [14]. The spectra of copper complexes exhibit a broad band around (600-755 nm) described by the ²Eg → ²T₂g electronic transition [15]. These transitions indicated the copper complexes to be distorted octahedral, the magnetic moment values of Cu complexes are (1.85-1.86) B.M [16-17]. The electronic spectrum of the zinc complexes gave bands at (303, 257 nm) and (408, 285 nm) in [Zn L₁Cl₂(H₂O)]
H₂O and [Zn L₂Cl₄ (H₂O)] H₂O respectively assigned to charge transfer. The complexes are diamagnetic which are expected for (d¹⁰- system) [18].

The electronic spectrum of manganese complexes showed three peaks: the first peak at (257, 247) nm was attributed to (⁶A₁g→⁴A₁g), the second peak at (301, 297) nm was attributed to (⁶A₁g→⁴T₁g) and the third peak at (302, 303) nm which was assigned to (⁶A₁g→⁴T₂g). These transitions indicated these complexes to be octahedral [18]. The molar conductances of the complexes (10⁻³M) in DMF refer to their non-electrolytic nature. The data are listed in Table 3. The suggested geometry of the complexes can be shown in Figures (1) and (2).

### Table 3: Electronic Spectra Data for the Prepared Metal Complexes.

| Compounds                  | (λ nm) | Assignment       | μe₀f [B.M] | Molar conductivity | Suggested geometry |
|----------------------------|--------|------------------|-----------|--------------------|--------------------|
| L1.L2                     | 248    | π→π⁺             | -         | -                  | -                  |
|                           | 311    |                  | -         | -                  | -                  |
|                           | 291    |                  | -         | -                  | -                  |
| [Cu L₁Cl₄ (H₂O)]H₂O       | 680    | ²Eg→²T₃g         | 1.92      | 16                 | O.h                |
|                           | 625    |                  |           |                    |                    |
|                           | 640    |                  |           |                    |                    |
| [Cu L₂Cl₄ (H₂O)]H₂O       | 600    | ²Eg→²T₃g         | 1.86      | 12.7               | O.h                |
|                           | 737    |                  |           |                    |                    |
|                           | 755    |                  |           |                    |                    |
| [Zn L₁Cl₄ (H₂O)]H₂O       | 303    | C.T              | 0.00      | 20                 | O.h                |
|                           | 257    |                  |           |                    |                    |
| [Zn L₂Cl₄ (H₂O)]H₂O       | 472    | C.T              | 0.00      | 12.3               | O.h                |
|                           | 285    |                  |           |                    |                    |
| [Mn L₁Cl₄ (H₂O)]H₂O       | 257    | ⁶A₁g→⁴A₁g         | 4.92      | 18.2               | O.h                |
|                           | 301    |                  |           |                    |                    |
|                           | 302    | ⁶A₁g→⁴T₁g         |           |                    |                    |
|                           |        | ⁶A₁g→⁴T₂g         |           |                    |                    |
| [Mn L₂Cl₄ (H₂O)]H₂O       | 247    | ⁶A₁g→⁴A₁g         | 4.88      | 11                 | O.h                |
|                           | 297    |                  |           |                    |                    |
|                           | 303    | ⁶A₁g→⁴T₁g         |           |                    |                    |
|                           |        | ⁶A₁g→⁴T₂g         |           |                    |                    |

Figure (1): Complex of 4-Nitro Benzophenone Sulfamethoxazole

Figure (2): Complex of Aceto Benzophenone Sulfamethoxazole
Conclusions:
Two Schiff bases were synthesized from sulfamethoxazole derivatives and characterized. The ligands were treated with metal ions salts to afford corresponding complexes. The complexes showed octahedral geometry around the metal.

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تحضير وتشخيص معقدات الزنك(II) والمنغنيز(II) مع ليكاندات جديدة من السلفاميثاكزول

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الخلاصة:
حضر الليكاندات 3-نايترو بنزوفينون سلفا ميثاكزول والليكاند بنزوفينون سلفا ميثاكزول من تفاعل السلفاميثاكزول مع كيتوانات مختلفة. شُخصت الليكاندات المحضرة بواسطة أطياف الأشعة تحت الحمراء فوق البنفسجية – المرئية والتحليل الدقيق لكعنصار(C,H,N) . تمت مفاعلة الليكاندات المحضرة مع أيونات النحاس والمنغنيز والزنك(ثانية التكافؤ) وشخصت المعقدات المحضرة بوساطة الطرق الفيزيائية المناسبة، (عوائق الامتصاص الذري أليبي واطياف الأشعة تحت الحمراء فوق البنفسجية - المرمية فضلا عن قياسات التوصيلية الكهربائية والحساسية المغناطيسية) ، ومن النتائج التي تم الحصول عليها فترى الشكل ثماني السطوح للمعقدات المحضرة.

الكلمات المفتاحية: سلفاميثاكزول، معقدات شيف، المعقدات الفلزية، مضاد للجراثيم.