

# New Cu (II) and Zn (II) complexes with O-nitrobenzylidene trimethoprim, Evaluation of their Antibacterial activities

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**Abstract.** Copper (II) and Zinc (II) complexes with O-nitrobenzylidene trimethoprim were prepared. The complexes were identified by employing Technique of CHNS analysis, molar conductance, magnetic susceptibilities and spectral measurements (FT-IR electronic spectra,  $^1\text{H}$  NMR,  $^{13}\text{C}$ -NMR). The above ligand formed ionic complexes having general formulae  $[\text{M}(\text{ONBTMP})_2]\text{X}_2$  in neutral medium and  $[\text{M}(\text{ONBTMP-H})_2]$  in basic medium,  $\text{M}=\text{Cu}, \text{Zn}$ ,  $\text{X}=\text{Cl}, \text{NO}_3, \text{SO}_4, \text{CH}_3\text{COO}$ , ONBTMP = ortho-nitrobenzylidene trimethoprim, hexa coordinated mononuclear, complexes were investigated by this study and having distorted octahedral geometries in Copper complexes and octahedral geometries in Zinc complexes. Then the antibacterial activity has been studied for both of ligand and all complexes by using agar plate diffusion techniques against "Pathogenic Bacterial strains {Staphylococcus aureus, pseudomonas aeruginosa, Proteus mirabilis, Escherichia coli and Bacillus subtilis}" [18]. Both of ligand and complexes were found to have antibacterial activity, better than of the primary article Trimethoprim.

**Keywords:** O-nitrobenzylidene trimethoprim, Trimethoprim Cu & Zn complexes, Antibacterial activity

## 1 Introduction

"Copper (II) & Zinc (II) are very important metals for health organisms, their complexes with Schiff bases which are synthesized from the condensation of primary amines with carbonyl groups that were used for preparation of new types of coordination chemistry compounds. They have been implemented as an important point in the development of Biochemistry and Inorganic Chemistry as optical materials" [1]. "Schiff base metal complexes have been widely studied. They have, Antimicrobial and biological applications" [2-4]. "Trimethoprim (TMP) [2,4-diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine] (Fig. 1), a synthetic broad-spectrum bacteriostatic agent, which inhibits bacterial dihydrofolate reductase belonging to a group of compounds known as diaminopyrimidines. The TMP Trimethoprim, can be used in complexation of some common drugs with metal ions" [5]. "The efficacy of the therapeutic agent is known to be enhanced upon coordination to a metal ion. The ability of metals to combine with ligands and then release ligands in some processes make them ideal for use in biological systems. Many drugs possess modified toxicological and pharmacological properties when they form metal complexes" [6].

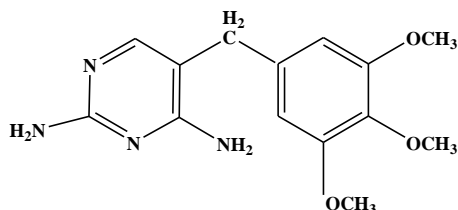


Fig. 1. (TMP) [2,4-diamino-5-(3,4,5-Trimethoxybenzyl) pyrimidine]

## 2 Experimental Starting Materials :

The Starting compounds are: ethanol, dimethylsulfoxide and acetic acid have been supplied from Merck. Trimethoprim, o -nitrobenzaldehyde, and all salts have been supplied by Aldrich

### 2.1 Preparation of ligand:

ONBTMP ligand (O-nitrobenzylidenetrimethoprim) (Fig. 2) has been prepared according to the literature [7] (Fig. 1) as follows: (5 gm, 0.0172 mole) ONBTMP was dissolved in 15 ml ethanol and then added to ethanolic solution of {2.60 gm, 0.0172 moles) ortho-nitrobenzaldehyd, respectively. The mixture has been refluxed for two and a half hour followed by evaporation to half their volumes then cooled. The residues were separated by filtration, washed with cold water and crystallized in hot ethanol. [ 7 ] eq. (1).

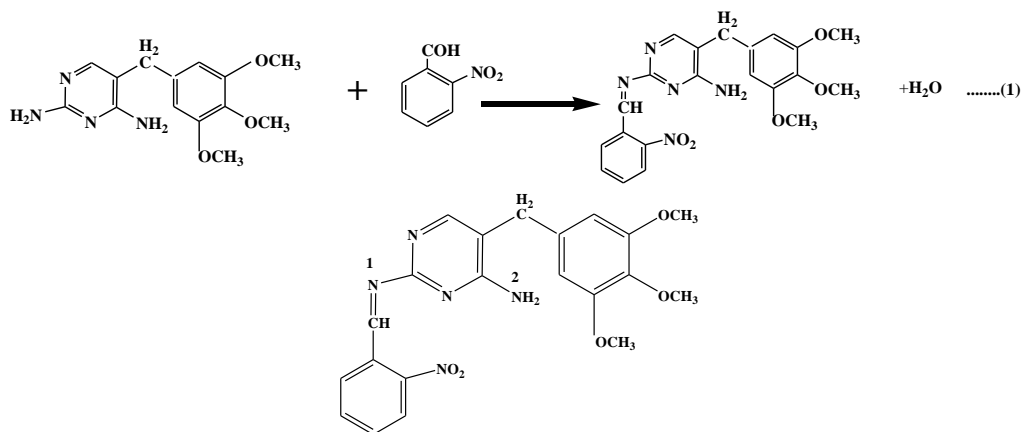


Fig.2. Model structure of ligand.

### 2.2 Preparation of the complexes

The reaction of Copper (II) and Zink (II) is carried out with O-nitrobenzylidenetrimethoprim ligand in a 1:2 molar ratio in both neutral and basic medium as follows: eq. (2) & (3)

## I- In a neutral medium :

$[\text{Cu}(\text{ONBTMP})](\text{NO}_3)_2$  has been prepared by dissolving of (0.438 gm  $1.03 \times 10^{-3}$  mole) of ONBTMP(O- nitrobenzylidenetrimethoprim )dissolved in 10ml of ethanol with  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$  (0.25g  $1.03 \times 10^{-3}$  mole) which dissolved in distilled water as ( 2:1 ) ratio. The mixture has been refluxed for three hours. evaporation to about half it's volume and then left to cool. The resulting complex was filtered off, washed with cold distilled water followed with diethylether and then dried. Complexes with the other Cu & Zn salts have been prepared using the same procedure [8] eq. (2) Fig 3 (Table 1)

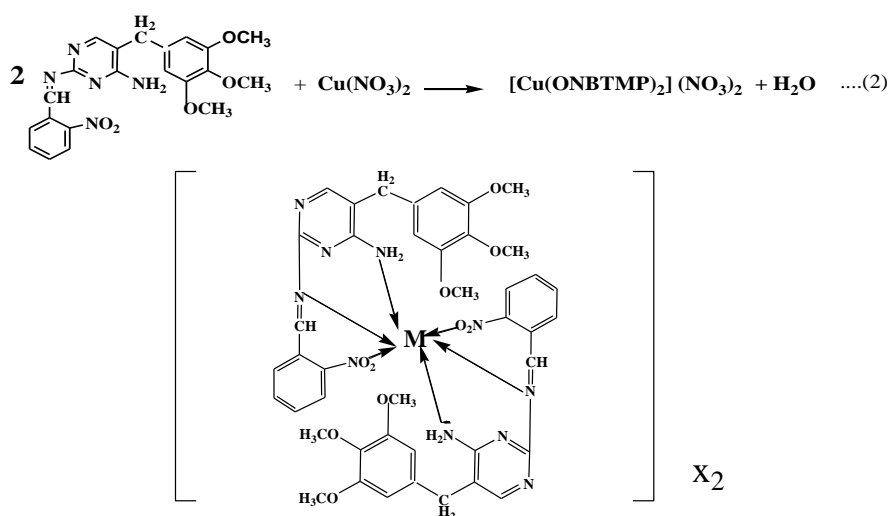
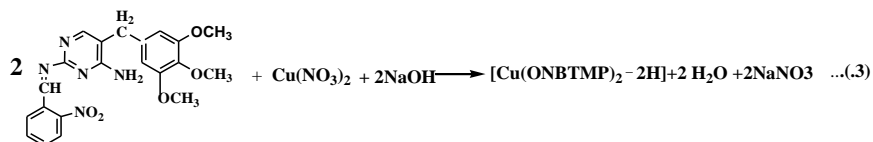
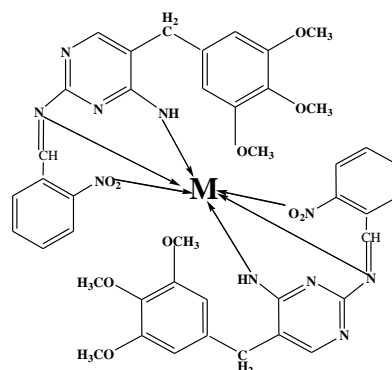


Fig.3. Complexes formula in neutral medium

## II- In basic medium:

Complex  $[\text{Cu}(\text{ONBTMP})](\text{NO}_3)_2$  has been prepared by the reaction of (0.438 gm  $1.03 \times 10^{-3}$  mole) of ONBTMP (O-nitrobenzylidenetrimethoprim )dissolved in 10 ml distilled water with ethanolic solution of  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$  (0.25g  $1.03 \times 10^{-3}$  mole as ( 2:1 ) ratio). The mixture was heated until a clear solution has resulted. Aqueous solution of sodium hydroxide (2M) was added dropwise to the mixture to reach pH=9-10. The product has been filtered off, washed with cold distilled water followed by diethylether and dried. All Complexes have been prepared using the same method above eq (3) Fig 4 (the amounts in grams were listed in Table 1)





**Fig.4.** Complexes formula in basic medium

**Table 1.** amounts, medium and formulae of the prepared complexes

NO.	Wt.of ONBTMP in gram	Salts 0.25 gm	Medium	% yield	Complexes
1	1.06	Cu(CH <sub>3</sub> COO) <sub>2</sub>	Neutral	86	[Cu (ONBTMP) <sub>2</sub> ] Ac <sub>2</sub>
2	1.06	Cu(CH <sub>3</sub> COO) <sub>2</sub>	Basic	76	[Cu (ONBTMP-H) <sub>2</sub> ]
3	0.876	Cu(NO <sub>3</sub> ) <sub>2</sub>	Neutral	81	[Cu(ONBTMP) <sub>2</sub> ](NO <sub>3</sub> ) <sub>2</sub>
4	0.876	Cu(NO <sub>3</sub> ) <sub>2</sub>	Basic	79	[Cu(ONBTMP-H) <sub>2</sub> ]
5	1.574	CuCl <sub>2</sub>	Neutral	86	[Cu (ONBTMP) <sub>2</sub> ]Cl <sub>2</sub>
6	1.574	CuCl <sub>2</sub>	Basic	76	[Cu (ONBTMP-H) <sub>2</sub> ]
7	1.326	CuSO <sub>4</sub>	Neutral	84	[Cu (ONBTMP) <sub>2</sub> ]SO <sub>4</sub>
8	1.326	CuSO <sub>4</sub>	Basic	76	[Cu (ONBTMP-H) <sub>2</sub> ]
9	0.964	Zn(CH <sub>3</sub> COO) <sub>2</sub>	Neutral	88	[Zn(ONBTMP) <sub>2</sub> ]Ac <sub>2</sub>
10	0.964	Zn(CH <sub>3</sub> COO) <sub>2</sub>	Basic	76	[Zn(ONBTMP-H) <sub>2</sub> ]
11	0.7117	Zn(NO <sub>3</sub> ) <sub>2</sub>	Neutral	89	[Zn(ONBTMP) <sub>2</sub> ](NO <sub>3</sub> ) <sub>2</sub>
12	0.7117	Zn(NO <sub>3</sub> ) <sub>2</sub>	Basic	92	[Zn(ONBTMP-H) <sub>2</sub> ]

### 3 Analytical and physical measurements:

The isolated complexes were analyzed for carbon, nitrogen, hydrogen, sulfur (CHNS) in Iraq–Baghdad –Ibn Al Haytham University

Molar refraction has been carried out. Conductivity measurements [9], magnetic susceptibility of the complexes, Electronic spectra infrared spectra of the ligand and its complexes the melting point, molar conductivity and electronic spectra, have been carried out. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR have been recorded for the ligand by NMR Bruker Ultra Shield 300 MHz in Lester University- UK using Deuterated DMSO.

### 4 Antimicrobial assay of the complexes

Four pathogenic microorganisms {Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Proteus mirabilis} were chosen to study the antibacterial activity

of the ligands and their complexes. All the bacterial strains have been carried out and identified in The Biology Department, College of Education for Pure Science, University of Mosul The antibacterial activity has been evaluated by agar plate diffusion technique [10]. against a variety of medicinally important gram-positive and gram-negative bacteria. In this method Nutrient agar plates have been seeded with 0.1 ml. of the nutrient broth culture of the tested microorganism containing ( $10^8$ ) cells/ml., Filter paper discs were impregnated with the tested materials then placed on the surface of seeded Nutrient agar plates, The plates were incubated at 37 °c for 24 hr., The zone of inhibition has been measured for the determination of minimum inhibitory concentration (MIC) [11] , Different concentrations of the tested materials (500, 250, 125 µg/ml) have been. the highest dilution which inhibits the growth has been recorded (Fig. 10). [11].

## 5 Results and Discussion

The resulting complexes were colored solids, air-stable, insoluble in water but soluble in DMSO Copper and Zinc relative molecular weights revealed that the complexes had the formula  $[M(ONTMP)_2]X_2$  in neutral and  $[M(ONTMP)_2-H]$  in basic medium. The ligand is tridentate. its coordinated to central metal ion by Oxygen atom of the nitro group which contain negative charge and the nitrogen atom of azomethen group and amine group, number (1,2 ) Fig [2]. [12] (Table 1). The values of the molar conductivities (70 -79 and 10-21  $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ ) approached those expected for 1:2 and non electrolytes. The molar refraction of the complexes in  $10^{-3}$  M DMSO solution was in the range  $1.4772 \times 10^{-4}$  -  $1.4876 \times 10^{-4}$  . (Table 2), The isolated complexes analyzed for carbon, nitrogen, hydrogen, sulfur (CHNS) ,Cu and Zn were determined by flame atomic absorption spectrometry (Table 3). The magnetic moments indicated the presence of one unpaired electron, for Copper(II) complexes [13], assigned to a monomeric structure, having distorted octahedral geometries in Copper complexes (Table 4).

**Table 2.** Some analytical and physical properties

No	Color	Mp C	ReF. $\times 10^{-4}$	M.Wt g/mol	$\Delta_M^*$
1	green	253	1.4773	1027.54	75
2	green	260	1.4775	907.54	19
3	green	211	1.4774	1033.54	74
4	green	220	1.4774	907.54	12
5	green	236	1.4775	980.54	70
6	green	231	1.4876	907.54	21
7	green	230	1.4876	1101.54	75
8	green	227	1.4773	907.54	10
9	yellow	215	1.4773	1029.4	79
10	yellow	211	1.4772	909.4	18
11	yellow	211	1.4775	1035.4	76
12	yellow	219	1.4775	909.4	15

$\Delta_M^*$  = molar conductance in  $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$

**Table 3.** CHNS analysis, Metal contents of the prepared complexes

No	C% (Exp.) Calc.	H% (Exp.) Calc.	N% (Exp.) Calc.	O% (Exp.) Calc.	S% (Exp.) Calc.	Cu % (Exp.) Calc.	Zn % (Exp.) Calc.
1	(52.65) 53.72	(5.01) 4.67	(13.11) 13.62	(23.10)21.80	-	6.18(5.98)	
2	(54.00) 55.53	(5.00) 4.40	(14.55)15.42	(19.00) 17.63	-	7.00(6.78)	
3	(47.91)48.76	(4.00) 4.06	(16.51) 16.25	(23.00)24.77	-	6.15(5.89)	
4	(55.11)55.53	(4.30) 4.40	(15.00)15.42	(17.01) 17.63	-	7.00(6.88)	
5	(51.35) 51.42	(4.13)4.28	(14.00) 14.27	(16.26)16.31	-	6.48 (5.96)	
6	(54.03)55.53	(5.00) 4.40	(15.35)15.42	(16.59) 17.63	-	7.00 (6.69)	
7	(49.98) 49.85	(3.10) 3.81	(11.03) 12.71	(25.21)26.14	(4.96) 5.81	5.77 (5.62)	
8	(55.06) 55.53	(4.02)4.40	(14.66)15.42	(16.01) 17.63	-	7.00 (6.39)	
9	(53.06) 53.62	(4.01)4.66	(13.11) 13.60	(20.09)21.76	-		6.35(6.09)
10	(55.14) 55.42	(4.14)4.39	(15.41)15.39	(17.05) 17.59	-		7.19 (6.97)
11	(49.01) 48.69	(4.11)4.05	(17.22) 18.47	(24.81)24.72	-		6.31 (6.20)
12	(55.20) 55.42	(4.16)4.39	(15.33)15.39	(17.35) 17.59	-		7.19(6.99)

**Table 4.** Magnetic susceptibility of the complexes

No.	D × 10 <sup>-6</sup>	M.wt	$\chi_g \times 10^{-6}$	$\chi_M \times 10^{-6}$	$\chi_A \times 10^{-6}$	$\mu_{\text{eff}}$ (B.M)
1	361.38	1027.54	1.10032	1130.62	1492.00	1.88
2	289.68	907.54	1.21130	1099.30	1388.98	1.81
3	339.20	1033.54	0.97431	1006.98	1346.18	1.79
4	289.68	907.54	1.10332	1001.30	1290.98	1.75
5	438.20	980.54	0.88733	870.06	1308.26	1.76
6	289.68	907.54	1.09867	997.08	1286.76	1.75
7	381.60	1101.54	0.81063	892.57	1274.17	1.74
8	289.68	907.54	1.06331	964.99	1254.67	1.73
9	363.58	1029.40	-	-	-	-
10	291.88	909.40	-	-	-	-
11	341.40	1035.40	-	-	-	-
12	291.88	909.40	-	-	-	-

The molar refraction is an additive and constitutive property. It has been used to construct the correct structure of the Copper(II) complexes [14]. The electronic spectra of the complexes in dimethylsulfoxide solutions have been recorded giving d-d transition and charge transfer spectra. Copper(II) complexes showed a wide absorption band at 14275 cm<sup>-1</sup> attributed to the accumulation of the two electronic transitions <sup>2</sup>E<sub>g</sub>→<sup>2</sup>B<sub>1g</sub> and <sup>2</sup>A<sub>1g</sub>→<sup>2</sup>B<sub>1g</sub>. The presence of this band strongly supported the octahedral geometry of the complexes, The higher ability of the stable state E<sub>g</sub> for the Jian-Teller effect, makes the Copper ion in their complexes showed distorted octahedral geometry [15]. The charge transfer band was observed at 33222-32733 cm<sup>-1</sup>. (Table 5)

**Table 5.** The electronic spectra of the Copper(II) complexes

N0.	$\nu_1$ (cm <sup>-1</sup> )	C. T. (cm <sup>-1</sup> )
1	14275	33057
2	14275	32840
3	14275	32840
4	14275	32733
5	14275	33222
6	14275	33222
7	14275	33057
8	14275	32733
9	-	-
10	-	-
11	-	-
12	-	-

## FT-IR

The infrared spectra of ONBTMP ligand (O- nitrobenzylidenetrimethoprim ) (Table 6) showed the band at 1688.60 cm<sup>-1</sup> due to  $\nu_{C=N}$  of Schiff bases (N1),(N)2, Fig 2 [16]. "On coordination this band was split into two bands, one appeared at the same position, whereas the other band observed at a lower frequency. This demonstrated that only one nitrogen atom was coordinated to the metal ion" [16]

The next band at 3401.13 cm<sup>-1</sup> attributed to  $\nu_{NH}$  remained unaltered for complexes prepared in neutral medium indicating that, there is no coordination through this group and the metal ion [ 16] in basic medium. This band disappeared due to the formation of the enolic form.

The other bands in the region 1344.72 cm<sup>-1</sup> in ligand and 1332.33 -1341.20 cm<sup>-1</sup> in complexes due to  $\nu_{C-O}$  of methoxy group remained unaltered upon coordination indicating that there is no coordination through these groups and the metal ion

The band at 1461.67 cm<sup>-1</sup> was attributed to  $\nu_{C-N}$  shifted towards a lower frequency which demonstrates that the imine nitrogen was coordinated to the metal ion (N1) Fig. 2

The spectra of Schiff-bases showed a strong band in the region 1688.60cm<sup>-1</sup> as due to C=N stretching vibration. This band shifted towards a lower frequency, which demonstrates that the imine nitrogen (N1) Fig 2 was coordinated to the metal ion

The band at 3080.79 cm<sup>-1</sup> in ligand below to aromatic C-H<sup>o</sup> and also in complexes the same band at 3192.18-3077.29 cm<sup>-1</sup> was observed.

The Band at 3401.13 cm<sup>-1</sup> in ligand below to  $\nu_{NH}$ , the bands between( 3312.62-3370.81) cm<sup>-1</sup> in complexes was observed at lower frequency, which demonstrates that the nitrogen atom was coordinated to the metal ion (N2 ) Fig 2

The Band at 1461.67 cm<sup>-1</sup> in ligand below to C-H of imine group. This band shifted towards a higher frequency, which demonstrated that the imine nitrogen (N1) fig 2 was coordinated to the metal ion [16]

The band at  $418.70 - 466.62 \text{ cm}^{-1}$  was due to  $\nu_{M-N}$ , and The band at  $455.65 - 526.23 \text{ cm}^{-1}$  was due to  $\nu_{M-O}$  which demonstrated that the oxygen atom of  $\text{NO}_2$  was coordinated to the metal ion by an oxygen atom. [16]



Fig .5. FT-IR For complex No. 1

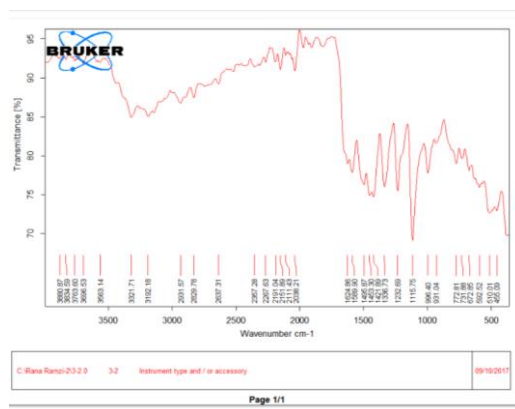
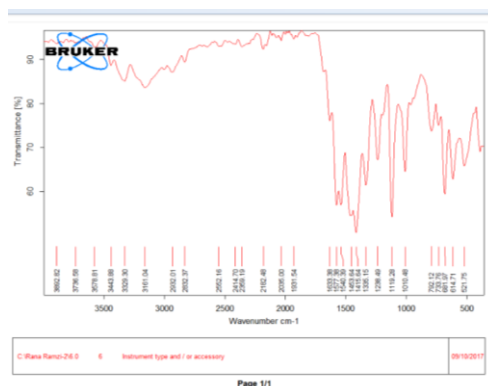


Fig .6. FT-IR For complex No.3.





**Fig.7.** FT-IR For complex No. 6

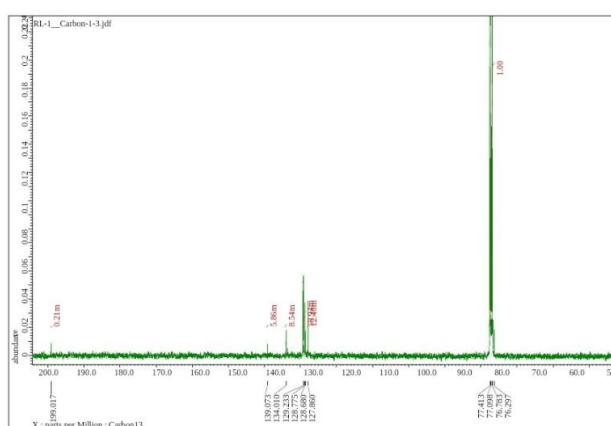
**Table 6.** Some Important Bands in FT- IR Spectra of the ligand and Their Complexes

**$^6$   $^1\text{H}$ NMR**

	$\nu_{\text{M-O}}$	$\nu_{\text{M-N}}$	$\nu_{\text{C=N}}$	$\nu_{\text{NH}}$	$\text{C-H}^\nu$	$\text{C=N}^\nu$	$\text{C-H}^\nu$	$\text{C-O}^\nu$	$\nu_{\text{C=N}}$	$\nu_{\text{-N}}$
ONB TMP	-	-	1461.67	3401.13	3080.79	1688.60	2939.58	1344.72	1582.22	1461.17
1	510.44	455.44	1524.19	3211.29	3211.29	1587.25	2936.51	1336.40	1587.25	1419.20
2	496.90	421.65	1499.87	3304.31	3077.03	1592.10	2933.31	1339.20	1580.98	1418.12
3	516.30	450.15	1495.87	3192.18	3192.18	1624.86	2931.57	1336.73	1589.90	1421.89
4	526.23	427.25	1688.89	3170.14	3170.14	1636.15	2941.66	1337.05	1588.89	1421.62
5	455.65	437.75	1647.91	3173.26	3173.26	1647.91	2935.33	1378.60	1590.28	1378.60
6	486.96	446.65	1633.38	3161.04	3161.04	1633.38	2932.01	1335.15	1577.38	1415.64
7	500.00	454.15	1633.79	3177.48	3177.48	1633.79	2834.31	1340.00	1586.61	1418.30
8	492.70	447.35	1620.81	3224.23	3180.14	1599.31	2931.21	1338.15	1582.90	1420.22
9	491.92	466.62	1590.99	3189.11	3201.25	1631.68	2935.58	1431.20	1588.21	1417.60
10	503.60	441.64	1612.41	3177.64	3160.34	1640.44	2931.92	1335.51	1584.26	1417.71
11	521.75	435.68	1607.01	3220.20	3191.29	1641.22	2931.26	1337.77	1578.13	1422.62
12	498.85	418.70	1598.08	3180.50	3171.55	1598.21	2938.14	1332.33	1589.28	1418.81

spectra of the ligand in Deuterated dimethylsulfoxide as internal reference were measured. The results of  $\text{H}^1$  NMR spectra supported the structure of the ligand under investigation [17].

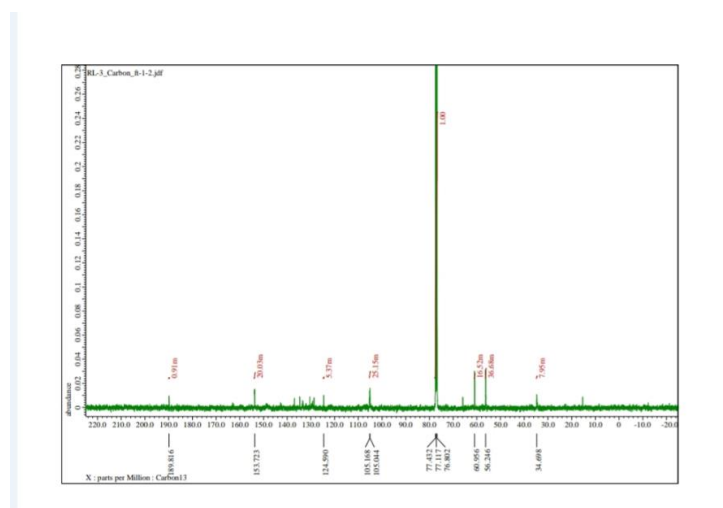
- . multi-signal at 1.3-1.2  $\delta$  belong to  $\text{CH}_2$
- . wide signal at 1.4-1.8  $\delta$  belong to  $\text{NH}_2$
- . the multi signal at 3.7-3.8  $\delta$  belongs to the methoxy group
- . single signal at 5.9-6.9  $\delta$  belongs to  $\text{N=C-H}$
- . the single signal at 7.24  $\delta$  belong to solvent  $\text{CDCl}_3$
- . multi-signal at 7.3-7.5  $\delta$  belongs to protons of aromatic ring
- . the single signal at 7.89-7.9  $\delta$  belong to C-H of pyrmedenine ring



**Fig. 8.**  $^1\text{H-NMR}$  (ONBTMP).

### $^{13}\text{C}$ - NMR

- . single signal at 153.7  $\delta$  belong to  $\text{N}=\text{C}$
- . multi signal at 124.5 , 132.3 , 135.5 , 136.5 , 139.5 145.6  $\delta$  belong to carbon of aromatic rings
- . single signal at 34.698  $\delta$  belong to  $\text{CH}_2$
- . signals at 55.1 , 56.24 , 60.95  $\delta$  belong to  $\text{C-OCH}_3$  [17]



**Fig. 9.**  $^{13}\text{C}$ - NMR ( ONBTMP)

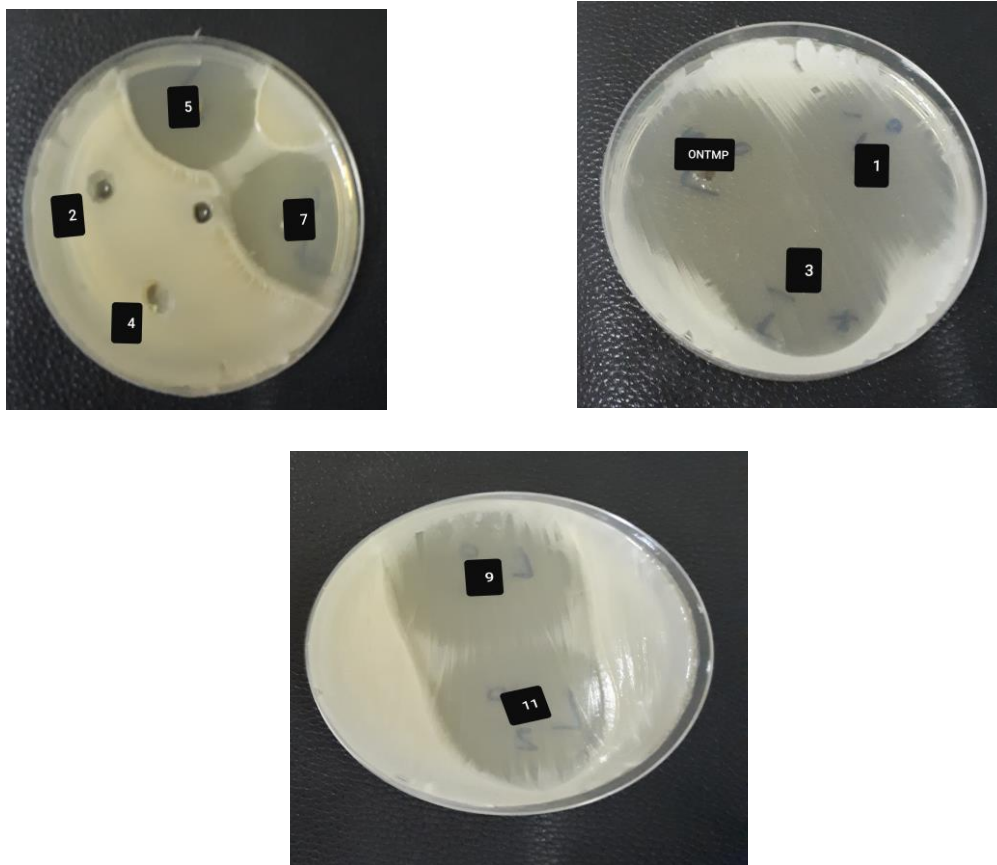
## 7 Biological Activity

Mostly all the chemical compounds are very efficient in attacking the bacteria during by synthesis of ribonucleic acid and could give results by the inhibition action of these compounds on the DNA of the bacteria of the activities of DNA gyrase enzyme including the separation of supercoiling or decantation or unkotting of the DNA [18-20]. "Moreover, the antibacterial is also known to attack the cell in different methods such as inhibiting the growth of microorganisms by affecting special target sites like the synthesis of the cell wall, protein and nucleic acid or by inhibiting the action of the cell membrane, binding of the sulfhydryl groups of the cell enzymes with the complexes" [21]. large number of experiments have been done to determine the antimicrobial influence of the complexes. Table (7 and 8, Fig. 4-6) showed that the ONTMP and number of complexes have antibacterial activity against the bacteria. As metal ion preferentially bind to  $-\text{N}=\text{C}$ ,  $\text{NO}_2$ , N of the ring in ligand effecting the cell enzyme more

strongly. " It is important to assume that the ligand and complexes screened were involved in competitive equilibria involving the  $-C=N-$  group of the cell enzyme. Therefore, we concluded that some of the compounds acquire biological activity. If this is the case, the compounds which were expected to bind to  $-NO_2$  group of the cell enzyme acted more strongly than the nitrogen donor atom in the ligand "[22](Table 7)( Fig 5),

**Table 7.** Antibacterial activity (inhibition zone) of different concentrations of the ligands and complexes ( $\mu\text{g/ml}$ ).

Compound	Pseudomonas auruginosa			Proteus mirabilis			Escherichia coli			Staphylococcus aureus		
	125	250	500	125	250	500	125	250	500	125	250	500
Cons\( $\mu\text{g}$	125	250	500	125	250	500	125	250	500	125	250	500
ONTMP	8	15	20	9	17	21	7	18	21	8	14	20
1	7	10	15	8	11	18	7	13	18	7	12	18
2	-	-	-	-	-	-	-	-	-	-	-	-
3	7	9	18	6	11	18	7	12	19	7	12	21
4	-	-	6	-	-	-	-	-	6	-	-	6
5	6	8	10	6	12	19	6	14	21	-	9	16
6	-	-	-	-	-	-	-	6	6	-	-	6
7	8	11	21	6	12	21	7	11	18	6	14	21
8	-	-	6	-	-	-	-	-	-	-	6	6
9	6	8	17	7	13	19	7	10	17	9	17	21
10	-	-	-	-	-	-	-	-	-	-	-	-
11	6	8	15	6	12	19	7	15	20	-	10	16
12	-	6	7	-	6	6	-	6	7	-	-	-
Ax25		-			-			-			9	
CIPS		10			10			10			10	
TMP		12			4			10			0	



**Fig. 10.** (inhibition zone) of ligand and some complexes

### References

- [1] Jindra, V. , Ladislav H.: Synthesis , structures and biological activity of copper (II) and Zinc (II) Schiff base complexes derived from aminocyclohexane-1-carboxylic acid. New type of geometrical isomerism in polynuclear complexes . *j.ica.vol.480* , 16-6 (2018)
- [2] Kumble, D., Geetha, M., Pinto, A : Application of metal complexes of Schiff bases as an Antimicrobial drug :A Review of Recent Works. *International Journal of Current Pharmaceutical Research*. Vol. 9, 0975-7066, (2017)
- [3] Abubakar, M. , Jabbi, M., Husaini, H., Nuhu, A. : Synthesis and characterization of schiff base of 3-[(2-Hydroxy-phenylimino)-methyl]-6-methoxy-quinolin-2-ol and its metal complexes and their evaluation for antibacterial and antifungal activity. *Algerian Journal of Engineering and Technology*. Vol.02,1-8 (2020)
- [4] Patil, R., Chaurasiya, R. : Synthetic, structural, thermal and biological studies of Zr (IV), Th (IV) and VO (IV) chelates with bis-bidentate Schiff bases. - *Asian J. Chem* Vol. 6 ,4615 ( 2008 )
- [5] .Hernández,D. , .Valdés ,C. & Ménerval · Z. : Synthetic clay mineral as nanocarrier of sulfamethoxazole and trimethoprim. *Applied Clay Science* ,

Vol.161, 395-403 (2018).

[6] Anacona, J. R. , Gil, C. C.: Synthesis and antibacterial activity of cefoxitin metal complexes... *Transit. Met. Chem.*, Vol. 30,605-609 (2005)

[7] Yass, I. A.: Synthesis of substituted 1, 3-Oxazepine and 1,3- Diazepine Via Schiff Bases for Sulfamethoxazole drug. *K. J. Pharm.Sci. N* Vol. 1,49-58 ( 2010)

[8] Vogel, A. I.: *Textbook of Practical Organic Chemistry* . Longman Green, London, 3<sup>rd</sup> Ed., 722 (1964)

[9] Al-Mukhtar, S. , Mustafa, I. A.: *Inorganic and Coordination Chemistry*. Arabic Version, Mosul Univ. Press., Mosul-Iraq (1988).

[10] Collins, C. H., Lyne , P. M. , Grange, J. M.: *Microbiological Methods* ; Butterworths, London. 6<sup>th</sup> Ed., 409 (1989).

[11]. Chakravarty, A. R.; Photocleavage of DNA by copper(II) complexes. *J. Chem. Sci.*; 118Vol.6, 443-453 (2006).

[12] Geary, W. J. :Use of conductivity measurements inorganic solvents for the characterization of coordination compounds. *Coord. Chem. Rev.* Vol. 7, 81 (1981).

[13] Kulaksizoglu, S., Gökçe ,C. , Güp, R.: Synthesis and characterization of bis(azine) ligands and metal complexes: DNA-interaction and extraction properties for metals and dichromate anions. *Turk. J. Chem.* Vol.36, 717-733 (2011).

[14] Kulaksizoglu, S., Gökçe, C. , Güp, R.: Asymmetric bis(bidentate) azine ligand and transition metal complexes: Synthesis, characterization, DNA-binding and cleavage studies and extraction properties for selected metals and dichromate anions. *J. Chil. Chem. Soc.*, 57Vol.3, 1213-1218 (2012).

[15] Gahlot, A., Sharma, S. , Mehta, R. K.: Cobalt(II), nickel(II), copper(II), zinc(II), Cadmium(II), dioxouranium(VI) and oxovanadium(IV) complexes with 2-(N-benzyl-2-hydroxybenzylideneimino) ethane sulphonic acid. *J. Indian Chem. Soc* Vol. 63, 198 (1986).

[16] Nakamoto, K.: *Infrared and Raman Spectra of Inorganic and Coordination Compound*. John Wiley and Sons, New York, 3<sup>rd</sup> Ed., 166-322 (1976).

[17] Jackman and Sternhell . :Application of NMR spectra in organic chemistry. Translated by Dr. Saeed m. sh. Mosul University (1984).

[18]. Kumar, L. Sh, Prasad, K. Sh. , Revanasiddappa, H. D.: Synthesis, characterization, antioxidant, antimicrobial, DNA binding and cleavage studies of mononuclear Cu(II) and Co(II) complexes of 3-hydroxy-N'-(2-hydroxybenzylidene)-2-naphthohydrazide. *Eur. J. Chem.*; 2Vol.3, 394-403 (2011).

[19] Rakhi ,C. , Shelly, S. : Synthesis, Spectral and Pharmacological Study of Cu(II), Ni(II) and Co(II) Coordination Complexes. *Res. J. Chem. Sci.* 1Vol.5, 1-5 (2011).

[ 20] Saif, M., Mashaly, M. M, Eid, M. F. , Fouad, R.: Synthesis, characterization and thermal studies of binary and/or mixed ligand complexes of Cd(II), Cu(II), Ni(II) and Co(III) based on 2-(Hydroxybenzylidene)thiosemicarbazone: DNA binding affinity of binary Cu(II) complex. *Spectrochim. Acta A. Mol. Biomol. Spec-trosc.* Vol. 92, 347-356 (2012).

[21] Khalaji, A. D., Gholinejad, M. , Triki, S.:The copper(II) complexes with tetradentate Schiff base ligands: Synthesis, crystal structures, and computational studies. *Russ. J. Coord. Chem.*. 39Vol.2, 209-213 (2013).

[22]. Jawetz, E., Melnick, J. L. , Adelberg, E. A. :Review of Medical Microbiology. Middle East Ed., Appleton & Lamage; Libieividu Liban ,17<sup>th</sup> Ed, 71-73, 136 (1987).