

PREPARATION, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF NEW AZO COMPLEXES CONTAINING PARACETAMOL MOIETY

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ABSTRACT

New sulfa drugs azo dyes () were prepared by the coupling of 4-acetamidophenol with some sulfa drugs (sulfadiazine Ld and, sulfaguinidine, Lg). The prepared ligands were characterized by F.T.IR-spectroscopy, ^1H and ^{13}C -NMR, Mass spectra, Micro-elemental analysis and UV-Vis spectroscopic techniques, magnetic, and conductance data. The ionization constants of the ligands and. The isolated complexes Ni(II), Cu(II) and Co(II) of azo ligands are found to have tetrahedral structure. The biological activity of the synthesized ligands and their metal complexes also are screened *K.pneumoniae*, *Proteus* spp. and *Ps.aeruginos* mortality were studied.

KEYWORDS: Azo-dyes ligand, chelate complexes, FT-IR, UV-Vis, ^1H , ^{13}C - NMR, antibacterial activity.

1. INTRODUCTION

Several studies have been published on the synthesis and spectral properties of azo dyes. This reflects their widely important applications in different fields such as coloring fiber^[1], photo electronic application^[6], optical storage technology^[7] sensitive chromomeric reagent^[8], sugar detection^[9] as well as their involvement in many biological reactions and in analytical chemistry.^[10] Azo metal complexes have also attracted an increasing attention due to their interesting electronic and geometrical features in connection with their application for molecular memory storage, nonlinear optical elements printing system^[11,12], also some of these organic dyes are used as antibacterial drug such as prontosil.^[12]

This study reports the preparation, characterization and antibacterial activity of new azo-ligand and its Ni(II), Cu(II) and Co(II) chelate complexes. Compounds ^1H and ^{13}C -NMR, Micro-elemental analysis and UV-Vis spectroscopic techniques, magnetic, and conductance data were done. The studies also included, acid-base properties, determination of ionization and protonation constants and their suggested mechanism.

Experimental

All the reagents and solvents were of reagent-grade quality. The progress of reaction was monitored by TLC using silica gel coated plates (0.5mm thickness, Merck) and spots were visualized under UV radiation. Infrared spectra (as KBr pellets) were recorded on F.T.IR-8400S Shimadzu. NMR spectra were recorded by Bruker ultra shield 300MHz spectrometer DMSO as solvent and TMS as internal reference. Melting points were determined by Buchi B190 K apparatus. Elemental analysis (C.H.N.), were carried out by Perkin element 2400. UV/Vis. absorption spectra of these compounds in different buffer solutions at room temperature were recorded using Perkin Elmer Lambda EZ 210 UV/Vis. Spectrophotometer.

To calculate the ionization and protonation constants for hydroxyl and nitrogen groups, a series of acetate and universal buffer solutions were prepared with different pH values^[0.5-12] for each organomercury compounds^[14]

Preparation of ligands^[15]

The azo ligand (Lg and Ld) with the structure depicted in figure 1 was prepared as described in the earlier methods for azo dyes. In short details, 1.61 g of **sulfadiazine Ld and, sulfaguinidine** was dissolved in 30 mL of water and 2.5 mL of concentrated hydrochloric acid to prepare 10 mmol solution. This solution was diazotized below 5 °C with 13 mL of aqueous sodium nitrite (1.0 mol. L⁻¹). A drop of the reaction mixture was tested from time to time with starch-iodide paper until nitrous acid persists in the solution for 10 min. The resulting diazonium chloride solution was added drop-wise with continuous stirring to **4-acetamidophenol** solution of 10 mmol concentration (1.44 g in 150 ml alkaline ethanol). The reaction mixture was stirred for 1 hr at 0-5 °C, and left in the refrigerator for overnight. The mixture was acidified with 0.1 N hydrochloric acid until the pH becomes 6. The soiled product was filtered off, washed with 500 mL cold water, air dried and recrystallized twice from hot ethanol and then dried in the oven at 80 °C for 6 hrs. fig 1,2 so

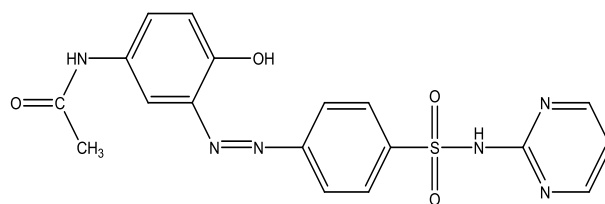


Figure 1 Structures of azo ligands Ld

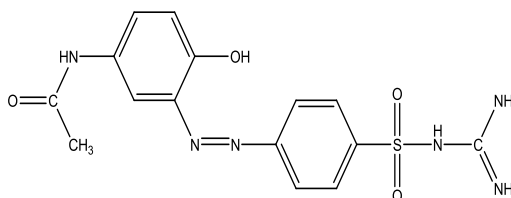


Figure 2 Structures of azo ligands Lg

Preparation of metal complexes^[16]

Synthesis of the complexes The appropriate metal chloride (Cu(II), Ni(II) and Co(II) ions) (10 mmol) in ethanol–water (1:1) (25 mL) mixture was added to the solution of the azo compound (0.40 g, 10 mmol) in the same solvent mixture (50 mL). The resulting solution was stirred under reflux for 0.5 h whereupon the complexes were precipitated. They were removed by filtration, washed with 1:1 ethanol/water and with Et₂O.

3-RESULTS AND DISCUSSION

Table 1: The analytical and the physical data of the ligands and their complexes

Comp.	Molecular formula	M.P ^o C	Analysis Found. (Calc)				Ω -1cm ² mol ⁻¹	$\mu_{eff.}$ (B.M.)
			N%	H%	C%	M% (Metal)		
Ld	C ₁₈ H ₁₅ O ₄ N ₅ S	229-231	20.49 (20.20)	1.47 (1.26)	52.71 (52.13)	-	-	-
LdCo	[Co(Ld)Cl ₂](H ₂ O)	300 ^o C >	15.55 14.48)	2.91 (2.41)	37.01 (37.24)	10.1 (10.1)	-	1.349
LdNi	[Ni(Ld)Cl ₂](H ₂ O)	300 ^o C >	15.01 (14.50)	2.46 (2.40)	37.44 (37.30)	9.7 (10.1)	24	1.977
LdCu	[Cu(Ld)Cl ₂](H ₂ O) ₂	300 ^o C >	15.13 (14.38)	2.66 (2.39)	37.11 (36.98)	10.4 (10.8)	33	1.666
Lg	C ₁₅ H ₁₅ O ₄ N ₆ S	235-237	14.22 (14.80)	4.11 (3.96)	48.02 (47.59)	-	-	-
LgCo	[Co(Lg)Cl ₂](H ₂ O)	300 ^o C >	15.80 15.44	2.71 2.57	33.08 33.00	10.5 (10.84)	8.8	1.435
LgNi	[Ni(Lg)Cl ₂](H ₂ O)	300 ^o C >	15.45 15.32	2.39 2.57	33.42 33.11	10.2 (10.7)	5.5	1.347
LgCu	[Co(Lg)Cl ₂](H ₂ O)	300 ^o C >	15.32 15.23	2.96 2.55	33.10 32.84	11.1 (11.5)	7.7	1.064

The compounds were prepared in good yield. The compounds are stable in air and light. Elemental analysis data and some physical properties of ligands and its complexes are summarized in table (1)

3.1. FT-IR Spectra

The most important IR absorption bands corresponding to the ligand and the complexes are presented in table 2. The observed band in the range 1450 cm^{-1} is due to ν (N=N) group of the ligand.^[14] These bands are shifted to higher region during the complex formation indicating its participation in coordination with the metal ions. The sharp band in the range 1521-1577 cm^{-1} are due to ν (C=C) respectively. The intense band was observed in the range 1622 cm^{-1} . The appearance of these bands medium support the involvement of -OH, and N=N groups in the formation of new azo ligand complexes. Some bands in the range of 470-480 and 530-567 cm^{-1} which are not present in the free ligands assigned to ν (M-O) and ν (M-N) vibrations.^[15] In all complexes the appearance

Table 2: IR frequencies (in cm^{-1}) of the azo ligands and their complexes

<i>Symb. of Comp.</i>	$\nu\text{C=O}$ cm^{-1}	$\nu\text{C=CAr}$ cm^{-1}	$\nu\text{C=N}$ cm^{-1}	$\nu\text{N=N}$ cm^{-1}	<i>M-N</i> <i>M-O</i>
Ld	1650	1577	1600	1423	-
LdCu	1690	1558.48	1653	1436.97	540 480
LdNi	1650	1525.69	1585.49	1417.68	567 480
LdCo	1653	1521.84	1581.63	1421.54	530 470
Lg	1664.5	1537	1622	1500	-
LgCo	1660 s	1566 s	1629 s	1427 s	560 530
LgCu	1660	1541	1627.92	1490	570 530
LgNi	1688	1537.27	1629	1443	540 490

3-2 -¹H and ¹³CNMR NMR spectra of ligands

¹H-NMR spectra of the prepared azo ligands were performed in deuterated dimethyl sulfoxide solutions with tetramethylsilane as an internal standard. All these spectra showed a peak at 2.5 ppm which was due to DMSO solvent. Figures (3 and 4) represent the, ¹H NMR spectra of the azo compounds and table 3 represents the data of these Figures^[15]

Table 3: ^1H -NMR data of the azo ligands

Comp.	δ (ppm)
Ld	2.6 (m., 3H, CH ₃) , 6.5-9 (m., 11H, Ar-H) 7.5 (m., 1H, NH) , 12 (br., 1H, NH) 10.1 (s., 1H, OH)
Lg	2 (m., 3H, CH ₃) , 6.5-8.5 (m., 7H, Ar-H) 7.3 (s., 1H, NH) , 6.5 (br., 1H, NH) 9.9 (s., 1H, OH) , 3.4 (m., 1H, NH) 10.6 (s., 1H, NH)

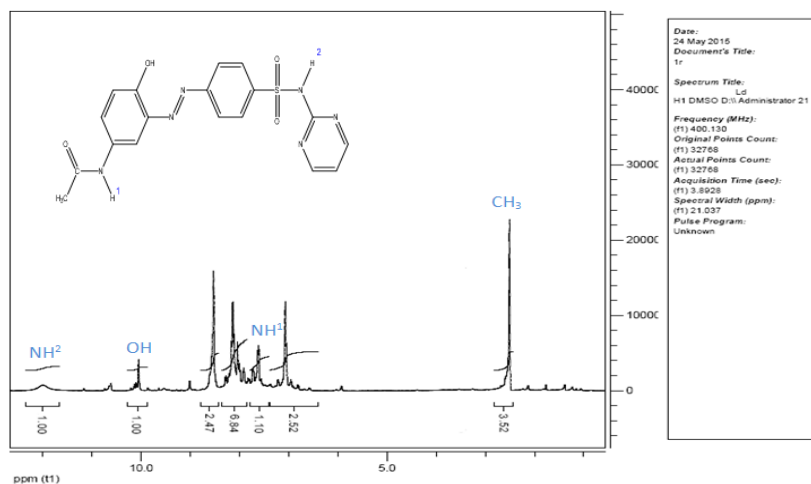


Fig.3: HNMR spectra for the Ld

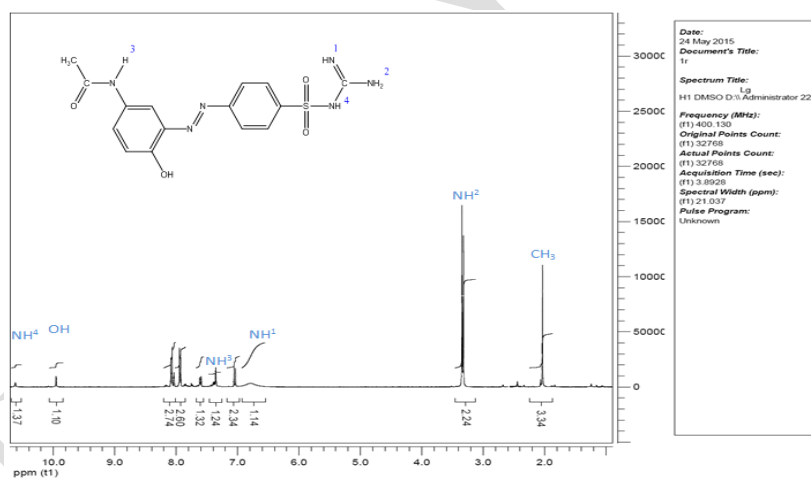


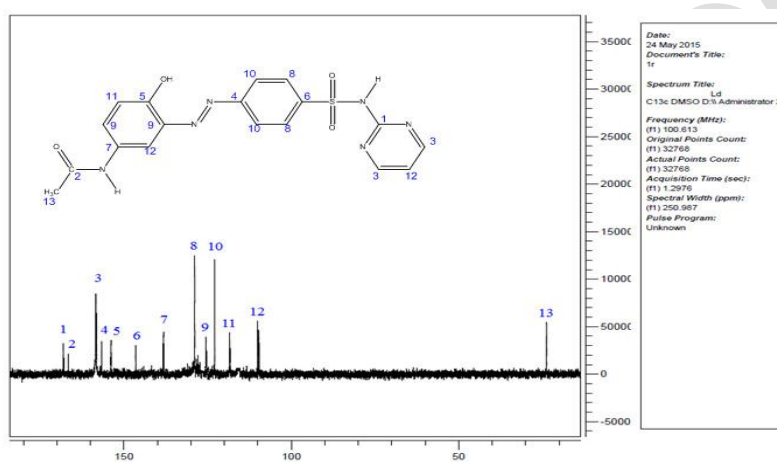
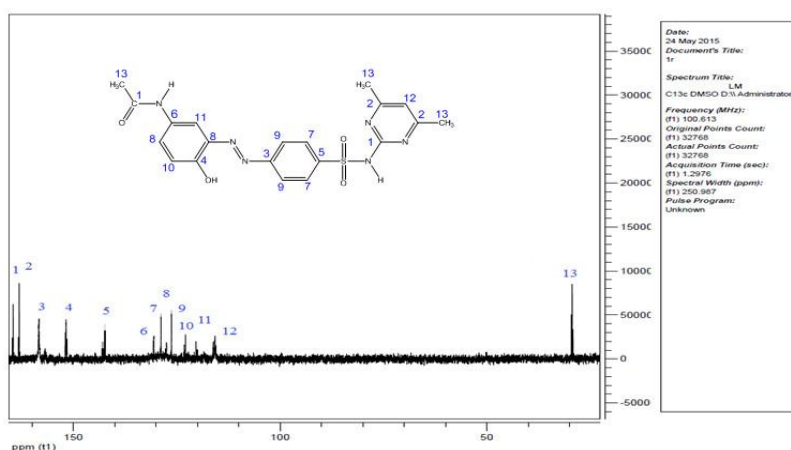
Fig4 : HNMR spectra for the Lg

The ^{13}C NMR Spectra of azo ligands are shown in table 4 and figures (5-6)

Table-4- ^{13}C NMR Spectra of azo ligands

Carbon atom	ppm) δ (Chemical shift)	
	Ld 	Lg

C ₁	168	174
C ₂	167	159
C ₃	158	158
C ₄	156	152
C ₅	154	151
C ₆	145	129
C ₇	140	127
C ₈	129	124
C ₉	126	123
C ₁₀	122	115
C ₁₁	119	110
C ₁₂	110	24
C ₁₃	22	---

Fig.5 : ¹³C-NMR spectra LdFig.6 : ¹³CNMR spectra spectra for the Lg

3-3 Electronic absorption spectra

The UV–Vis spectral data of the ligands and their complexes are given in table 5. The aromatic peaks of (Ld and Lg) ligand at (320-330), (240-) nm, which may be ascribed to,

$n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$, intra ligand charge transfer transitions respectively, due to presence of conjugation in the ligand molecule. The electronic spectra of the azo ligand complexes show two intense transition peaks < 400 nm which are assigned to ligand centered transitions, along with intense peak at longer wavelength (490-510) nm that can be referred to the combination of MLCT [$d\pi(M^{2+}) \rightarrow \pi^*(L)$] transitions where $\pi^*(L)$.^[14-17]

Table-5 The electronic spectra of of the azo ligands and their complexes

Compound	phenyl Cycle *) $\pi \rightarrow \pi^*$ ()nm(-N==N- *) $\pi \rightarrow n$ ()nm(-N==N- *) $\pi \rightarrow \pi^*$ ()nm()T-C()nm(
Ld	250	330	410	
LdNi	250	310		510
LdCu	260	320		520
LdCo	250	320		530
Lg	240	330	430	-
LgNi	250	320	-	520
LgCu	240	320	-	490

3.4 Determination of the proton-ligand ionization constants

The ionization constant of the ligands were determined potentiometrically using the Irving-Rossotti technique^[18-19] at constant temperature 25 °C. The values of the average number of protons associated with the ligands nA at different pH values were calculated. The proton-ligand formation curves are obtained by plotting nA versus pH at constant temperature.

Table-6 : The ionization and protonation constants of Ligands

pKa ₂	pKa ₁	pKp ₂	pKp ₁	λ_{max} nm	الرمز
10.6	8.4	-	3.4	520	Ld
-	8.3	-	-	520	Lg

Ka= ionization constant of -OH group pkp= protonation constants

The molar conductance values of the coordination compound of mentioned metal ions under investigation were determined using (1.0×10⁻³ mol. L⁻¹) DMF solvent, as showed in table 1 are in the range of (10- 14) S. cm².mol⁻¹. These values suggest the presence of a non-electrolyte.^[20] The magnetic moments of Ni(II), Cu(II), and Co(II), complexes were measured at room temperature and the obtained values are listed in table 1.

The Co(II) complex exhibited the magnetic moment value lies in the range of 1.433-1.345 BM corresponding to three unpaired electrons which suggests an square planer geometry.^[21]

The magnetic moment observed for Ni(II) complex lies in the range of 1.977-1.347 BM, which is consistent with the tetrahedral stereochemistry of the complex.^[22] The Cu(II) complex exhibited a magnetic moment value lies in the range of 1.66-1.064 BM, slightly lower than the spin-only value of 1.73 BM expected for one unpaired electron suggesting the possibility of an tetrahedral geometry.

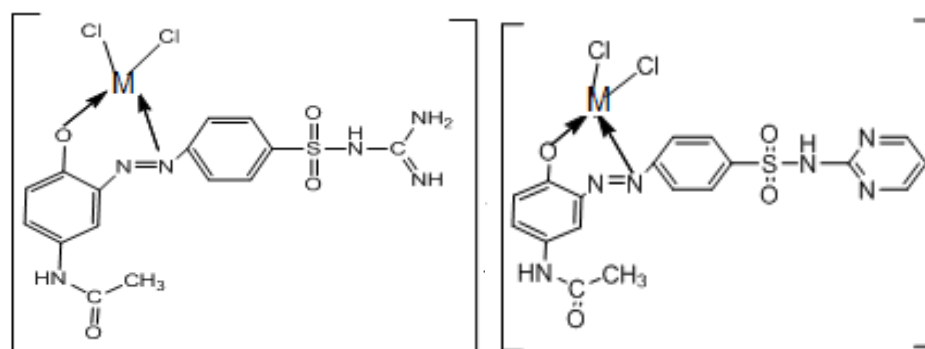


Figure 7: The suggested geometry of Co(II), Ni(II) and Cu(II) Chelate complexes for Ld and Lg

The antibacterial effect of the ligands and their complexes against both gram positive and gram negative bacteria was measured and tabulated in table (7). On chelation, the orbital of each metal ion is made so as to overlap with the ligand orbital. Increased activity enhances the lipophilicity of complexes due to delocalization of π – electrons in the chelate ring. In some cases increased lipophilicity leads to breakdown of the permeability barrier of the cell.^[23]

Table 7: Antibacterial activity data (zone of inhibition in mm) of ligand and metal complexes

Isolates chemicals	<i>S.aureus</i> IZ(mm)	<i>E.coli</i> IZ(mm)	<i>K.pneumoniae</i> IZ(mm)	<i>Proteus spp.</i> IZ(mm)	<i>Ps.aeruginosa</i> IZ(mm)
Lg	-	-	-	-	-
Ld	-	-	-	-	-
LgNi	-	-	-	-	-
LdNi	11	-	-	-	-
Lgco	-	-	-	-	-
Ldco	-	-	-	-	-
Lgcu	-	-	-	-	-
Ldcu	-	-	-	-	-

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