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SYNTHESIS AND SPECTRAL CHARACTERIZATION OF SOME TRANSITION METAL COMPLEXES OF AZO-SCHIFF BASE DERIVATIVE OF METOCLOPRAMIDE

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ABSTRACT

A new Azo-Schiff base ligand L was prepared by reaction of azoaldehyde with Metoclopramide (2-(diethylamino)ethyl 4-aminobenzoate). This synthesized ligand was used for complexation with different metal ions like Ni (II), Co (II), Cu (II) and Cr (I11) by using a molar ratio of ligand: metal as 2: 1. Resulted compounds were characterized by NMR (1 H), UV–vis spectroscopy, FT-IR, MS, elemental analysis, and molar conductivity studies. The synthesized ligand and metal complexes were screened for antibacterial activity against some Gram-positive and Gram-negative bacteria.

KEYWORDS*:* Schiff bases; azo compounds; Metoclopramide, antibacterial and activity.

INTRODUCTION

Azo Schiff base complexes contain both azo and azomethine groups. Azo compounds serve as important analytical tools by providing a strongly chromophoric label, theconcentration of which is easily determined by colorimetric, spectrophotometric or spectrofluorimetric methods. Besides, azo compounds are important analytical aid compounds serving as pH indicators, complexometric indicators and to a lesser extent, pre-concentration reagents.[1] The pharmacological use of azo compounds originates from the discovery of the antibacterial action of Prontosil on streptococcal infections by.[2] Furthermore, azo compounds were reported to show a variety of biological activities including antibacterial[3], antifungal[4], pesticidal[5], antiviral and anti-inflammatory activities.[7]

Schiff base derivatives attract significant interest and occupy an important role in the development of coordination chemistry. Moreover, Schiff base complexes containing transition metals have been studied in several research areas such as structural chemistry[8], Schiff bases are used as substrates in the preparation of a large amount of bioactive and industrial compounds.[9-13] In addition, Schiff bases are well-known to have biological activites such as antibacterial[14-15], antifungal[16-17], antitumor[18-19], antiviral[20-21], anti-HIV-1[22], antiproliferative[23], herbicidal[24] Schiff bases derived from salicylaldehydes are known polydentate ligands, coordinating to metals in both their deprotonated and neutral forms[25,26] Some cobalt and copper complexes exhibit diverse biological properties viz. anti-inflammatory, antibacterial and anticancer.[27]

This study reports the preparation, characterization and antibacterial activity of new azo-schiff base ligand and its Ni(II), Cu(II)), Co(II) and Cr(III), chelate complexes. Compounds 1H, Micro-elemental analysis and, UV-Vis spectroscopic technique, and, Conductance data. were done. The studies also included, acid- base properties, determination of ionization and protonation constants.

Experimental

General

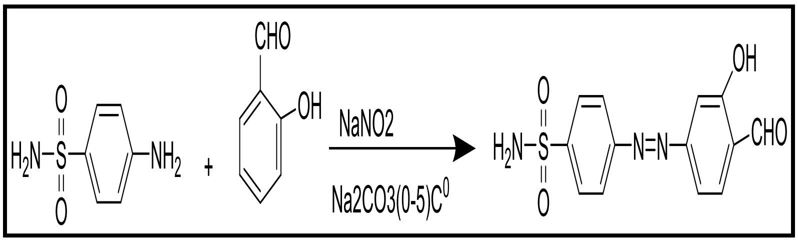
All the reagents and solvents were of reagent-grad quality, The progress of reaction was monitored by TLC using silica gel coated plates (0.5mm thickness, Merck) and spots were visualized under UV radiation. Infrared spectra (as KBr pellets) were recorded on F.T.IR-8400S shimadzu. NMR spectra were recorded by Bruker ultra shield 300MHz spectrometer DMSO as solvent and TMS as internal reference. Elemental analysis (C.H.N.), were carried out by Perkin element 2400.UV/Vis. absorption spectra of the these compounds in different buffer solutions at room temperature were recorded using Perkin Elmer Lampda EZ 210 UV/ Vis. Spectrophotometer. To calculate the ionization and protonation constants for hydroxyl and nitrogen groups, aseries of acetate and universal buffer solutions were prepared with different pH values(2-12).[28]

Preparation of ligand[28-30]

Synthesis of the azo dye compound (Z)

The azo dye compound Z been synthesized by the diazotization coupling reaction by flowing methods proposed (schem-1) Sulphanamide (1.33 gm, 0.01mol) was dissolved in mixture a solution from 3ml HCl(37%) and 30 ml distilled water. An aqueous solution 20 ml of NaNO2

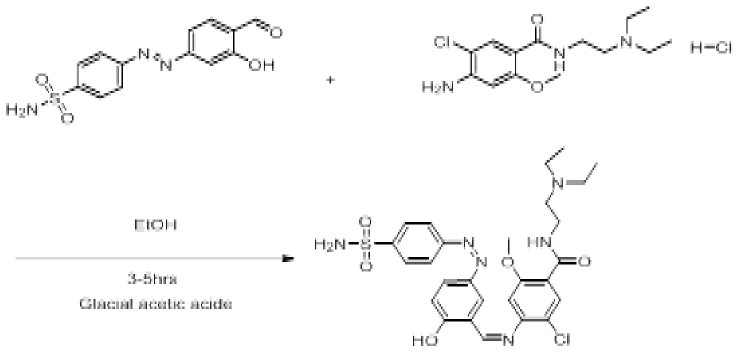
(0.75 gm, 0-0.1mol, dissolved in 20ml distilled water) was added in drops while maintaining the temperature between 0-5°C to the mixture with continuous stirring. After that the diazonium chloride was added drop wise respectively with constant stirring to cold aqueous solution of Salicylaldehyde (1.2gm,0.01mol) and then solution of 2ml acetic acid was added to the dark red colored mixture. The mixture was stirred for 1 hour at 0-5°C. The precipitate was filtered and washed with distilled water and 5ml ethanol solution to remove the excess of unreacted substances and recrystallized from ethanol and dried in oven at 50°C for several hours. The purity was confirmed by the elemental analysis (C.H.N) and TLC techniques. The yield was 82% of dark red crystals and m.p=177°C. The structure of azo compound (Z) is convert by, IR and UV-vis. spectra.



Scheme 1: preparation of noval azo compound.

Synthesis of novel azo-Schiff base ligand (L)

The novel azo-schiff base ligand (L),(scheme 1) was synthesized by condensation of Metoclopramide (2-(diethylamino)ethyl 4-aminobenzoate) (0.01 mole) with azo dye compound Z (0.01 mole) in 70 ml ethanol in the presences 4 drops of glacial acetic acid as a catalyst. The mixture refluxed for three hours, then the obtained product was concentrated in vacuum to remove ethanol. A Brown color precipitate were obtained, Which were filtered and washed with distilled water and twice recrystallized from hot ethanol, then dried in oven at 70°C for several hours. The yield 78% of reddish orange crystals and m.p=185°C.The purity was confirmed by the elemental analysis and TLC techniques. The structure of azo Schiff base ligand (L) is convert by 'H-NMR, mass spectrum, IR and UV-visb. spectra.



Scheme 2: preparation of noval azo-schiff base ligand.

Synthesis of azo Schiff base chelate complexes

The reaction of azo Schiff base by dissolving the ligand (L) in 50ml thanol(0.002mole) with (0.001 mole) of metal salts of $CoCl_2.6H_2O$,$NiCl_2.6H_2O$, $CuCl_2.2H_2O$,$CrCL_3.6H_2O$] respectively in a molar ratios 1:2 [metal: Ligand]). This metals chlorides dissolved in 50 ml of methanol were refluxing with stirring for 30 mint, colored precipitate formed at room temperature, than the resulting solids were filtered and washed several times with distilled water. The chelate complexes were dried in air and recrystallized from ethanol and dried in the oven at 70°C for several hours.

RESULTS AND DISCUSSION

All the prepared complexes in this paper were insoluble in water but soluble in DMSO. The range of conductance values in DMSO which are listed in table 1 indicates that all the metal complexes have a non-electrolyte nature except Cr complex. The physical properties and elemental analysis data are listed in Table 1.

Table 1: Physical properties, conductivity and analytical data of the free ligand and its complexes.

Comp.	Chemical Formula	M.P^0 C	Yield %	C%found (calc.)	H%found (calc.)	N%found (calc.)	Cond. S cm2 mol−1
Z	$C_{13}H_{11}N_3O_4S$	177	60	51.43 (51.14)	3.42 (3.65	13.76 12.96	-
L	$C_{26}H_{29}ClN_6O_4S$	269	62	56.06 (56.40)	5.25 5.50	15.09 14.89	-
M_1	$[Cu(L)_2]$	>300	61	53.16 (53.50)	4.6 4.32	23.51 23.65	17
M_2	$[NiL)_2]$	>300	65	53.42 (53.94)	4.62 4.93	23.61 23.30	15
M_3	$[Co(L)_2]$	296	60	53.37 (52.70)	4.81 5.081	23.60 24.11	18
M_4	$[Cr(L)_2(H_2O)_2]Cl$	>300	66	53.69 (53.30)	4.64 4.33	23.74 24.07	37

The FTIR

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 1521-1577cm-1 are due to ν (C=C) respectively(fig -1). 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 form ation 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 ligand assigned to ν (M–O) and ν (M–N) vibrations.[28] appearance In all complexes).

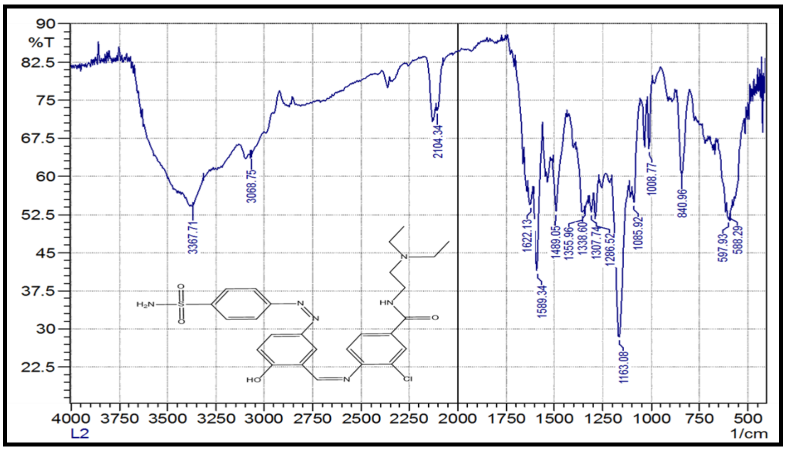


Fig. 1 I R Spectra of L.

Table 2: Selected infrared and uv.visible data of Z, L and complexes.

Comp.	ν(OH)	ν(N=N)	υ(C =C)	ν(C=N	υ(M–O)	υ (M-N)	UV-Vis spectral λ_{max} π-π^*) (n-π^*) C.T d-d
Z	3365	1477 1487	1589	-	-		272 351 242
L	3429	1489	1589	2812	-	-	298 358
M_5	3421	1444	1593	2968	590	470	288 380 459 691
M_6	3414	1454	1597	2906	590	485	291 387 456 730
M_7	3420	1444	1593	2968	590	450	244 363 460 680 272
M_8	3427	1417	1583 1528	2937	588	465	298 370 456 687

Electronic absorption spectra

The UV–Vis spectral data of the ligands and their complexes are given in table 2. The aromatic peaks of () ligand at(350-380) and (240-298) nm, which may be ascribed to, n→π* and π →π*, intra ligand charge transfer ransitions respectively, due to presence ofconjugation in the ligand molecule. The electronic spectra of the ligand complexes showtwo intense transition peaks < 440 nm which are assigned to ligand centered transitions, along with intense peak at longer wavelength (450-460) nm that can be referred to the combination of MLCT [dπ(M2+)→π*(L)] transitions where π*(L).[29]

Transitions at680-730nm can be referred to the d-d transition.

NMR

1H-NMR spectra of the prepared (L) were performed in deuterated dimethyl sulfoxide solutions with tetramethylsaline as an internal standard. spectra showed a peak at 2.5 ppm which was due to DMSO solvent. Figures (2) represent the, 1 H NMR.

spectra of the azo-Shiff base and table(3) represents the data of the Figure.[28]

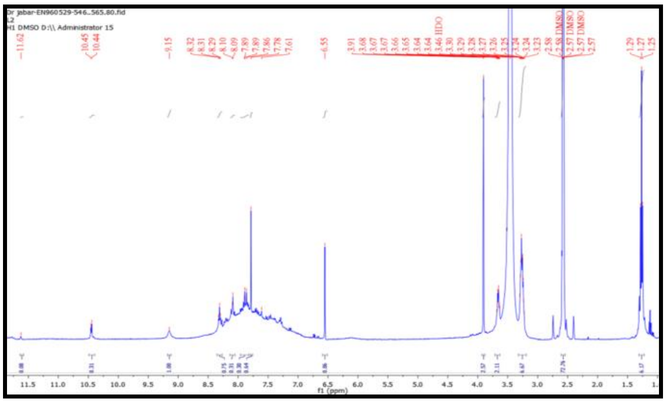


Fig. 2: HNMR spectra for the L.

Table 3: 1H -NMR data of the azo –schiff base (L).

Comp.	**δ (ppm)**
CH_3 (methyl)	1.2
CH_2 (methylene)	2.46-3.6
CH(1-benzene)	7.2-8.3
CH (azomethine)	8.38
NH (amide)	8.34
CH(1-benzene)	9.2
OH	10.5
NH (amine)	11.6

Mass spectrum

The electron impact spectrum of compound (L) confirms the probable formula by showing a peak at 587.1 *m*/*z*, corresponding to molecular ion [$C_{26}H_{29}ClN_6O_4S$], scheme 3 show the mechanim of fragmentation.

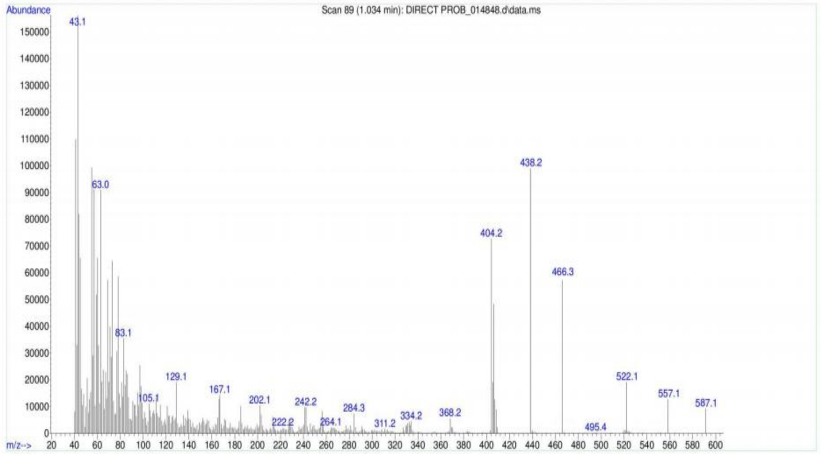
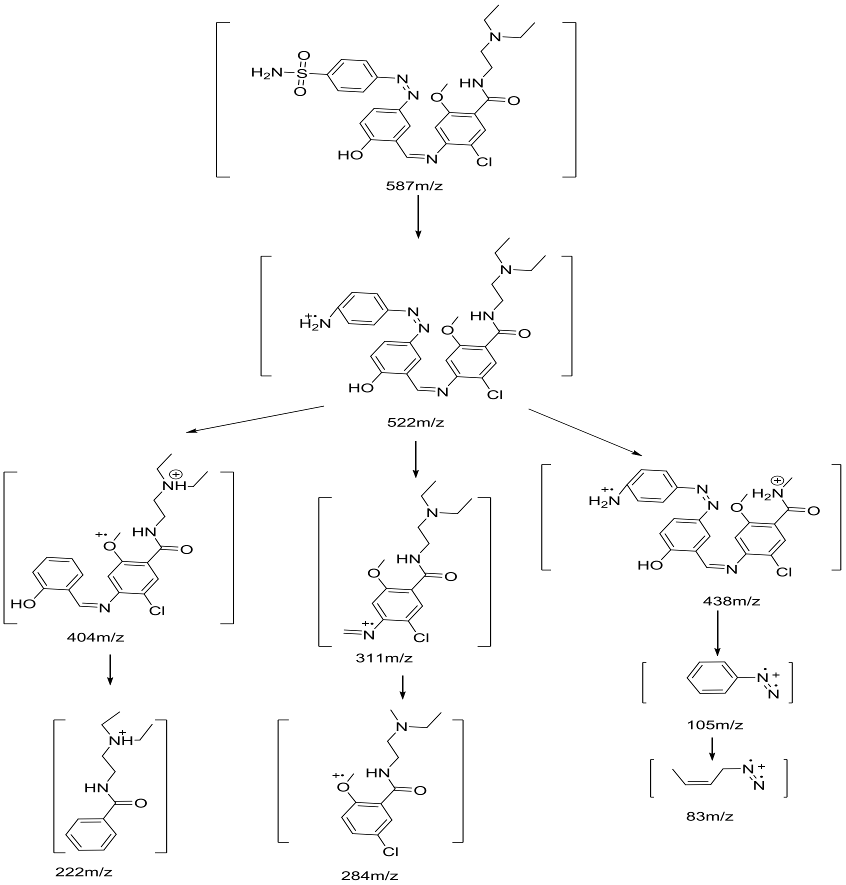


Fig. 3: Mass spectra for the L.



Scheme 3-Fragmentation of L.

Molar Conductivity Measurements

By using the relation Λm = K/C, the molar conductance of the complexes (Λm) can be calculated, where C is the molar concentration of the metal complex solutions, K = specific conductivity of the complex. The chelates were dissolved in DMSO, the molar conductivities of 10−4 M of their solutions at 25˚C ± 2˚C were measured. Table (1) these complexes are non-electrolytes[27] Except Cr(III), complex, it has molar conductance of 37 Ω−1·mol−1·cm2 indicating electrolytic nature (1:1)of the complex.[28]

Acid. Base Propcrtics of azoaldehyde

In the visible region. The absorption spectra of (0.8 × 10-4M) solution of azoaldehyde Z at varying pH value (2-12) fig 4. The spectra characterized two maximal bands 410 and 440 nm for L,. The first bands due to the absorption of the protonated form liable to exist in acid solution and the second bands is due to ionic form of dyes at basic solution. The absorption spectra were characterized by the presence of three isobestic points at (370nm), The three isobestic points are due to the ionization of dyes in acidic and basic medium From Absorbance vs pH and fron half height method[29] the pk values of ionization and protonation were obtained pka values of ionization**,** pkp protonation **constant.**

	$\lambda_{max)}$ nm	$A_{1/2}$	PKp		$A_{1/2}$	PKa
Z	370	1.829	6.5		1.845	9.5

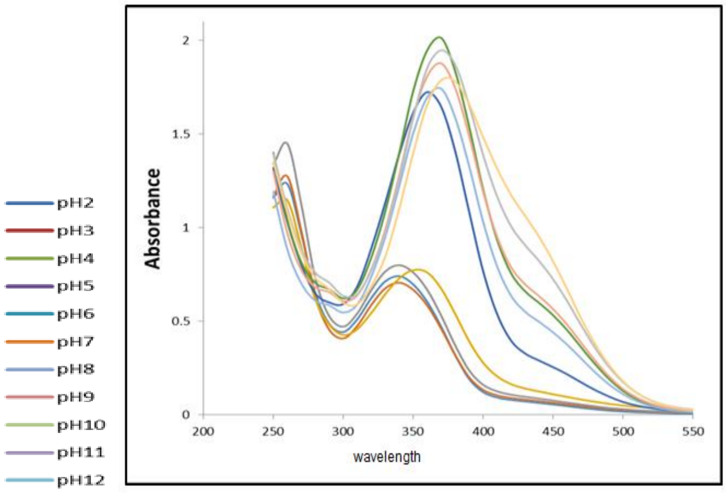


Fig. 4: Spectra of azodye at different pH.

Biological Studies[30]

The organisms used in the present investigation included Gram positive bacteria (*Staphylococcus aureus*) and Gram negative bacteria (*Escherichia coli*). The results of the bactericidal screening of the synthesized compounds are recorded in Table 4. An influence of the central ion of the complexes in the antibacterial activity against the tested Gram positive and Gram negative organisms show that the Z, have an enhanced activity compared to the its complexes.

Table 4: Antibacterial activity data of azo,ligand and its complex inhibition zone (mm).

Comp.	**Inhibition zone (mm).**	
Z	**E.coli 5mg/ml**	***Staphylococcus aureus* 5mg/ml**
	23	*17*
L	21	23
$[Ni(C_{26}H_{29}ClN_6O_4S)_2]$	21	**17**

CONCLUSION

New CoII, NiII, CuII, andCr(III**),** metal complexes with Azo-Schiff base derived L from reaction of azoaldehyde with Metoclopramide (2-(diethylamino)ethyl 4-aminobenzoate) have been synthesized. All the complexes are insoluble in water but soluble in DMF, as well as all of them are non-electrolyte. The structure of the complexes based on Uv-Vis, IR, mass spectroscopy were proposed that the Azo-Schiff base Ligand L behave as bidentate which coordinated with the metal ions through N, O atoms. The synthesized ligand and its metal complexes were screened for their biological activity against bacterial species, Gram positive bacteria (*Staphylococcus aureus*) and Gram negative bacteria (*Escherichia coli*).

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