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Synthetic, Structural, Magnetic, TGA and biological Studies of Some Copper Complexes of heterocyclic Schiff Base ligands

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ABSTRACT

Solid complexes of Cu(II) with Schiff base ligand derived from substituted trizoles have been synthesized. They have been characterized by elemental analysis, molar conductance, IR, ^{1}H-NMR and UV spectra and TG analysis and Probable structures are assigned to the complexes. Physicochemical data suggest octahedral geometry to Cu(II) complexes . The IR spectra of the ligands and their complexes are used to identify the type of bonding. The TG analysis of ligands and their Cu(II) complexes have been carried out. The free ligand and its Cu(II)complexes have been tested for their possible antibacterial activity against *E. coli and S. aureus* by cup plate method.

Keywords: 1, 2, 4- Triazole , Cu(II) complexes, Magnetic, TGA, biological Studies

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INTRODUCTION

The Chemistry of Heterocyclic Compounds is branch of Chemistry that dealing with synthesis properties and application of heterocyclic compounds. Heterocyclic compound are very important in field of medicinal Chemistry [1]. Nitrogen based Heterocyclic compound are very important in field of medicinal Chemistry they have very good biological activities [2, 3]. Azoles are important five membered heterocyclic rings containing at least one nitrogen atom like Isoxazole, Thiazole, Pyrazole and Triazole [4-6]. Moreover sulphur containing heterocyclic represent an important group of sulphur compounds that are promising for use in practical applications antifungal, antitubercular [7]. The importance of metal complexes of 1,2,4- Triazole amide in academic commercial and pharmacological fields provoked our interest in the co-ordination chemistry of 1,2,4-Triazole. This has led to systematic study of Cu(II) metal complexes of 1,2,4-traizle4-yl isonicotinamide derived from substituted Oxiadiazole and isonicotinic acid hydrazide. The therapeutic effects of 1,2,4-triazole and 1,2,4-triazole 3-one containing compound have been well studied for a no of pathological condition including cancer, pain, tuberculosis or hypertension [8]. Copper II ions is a biologically active in chelating ability and biologically transport reaction Cu(II) complex possess wide range of biologically activity and are among the most potent antiviral, antitumor and antiflammatary agents [6, 8]. In the present work, six isonicotinamide ligand and their copper complex have been prepared and characterised.

EXPERIMENTAL

All the chemical use as starting material for synthesis of the ligand and their metal complexes where A.R. grade or chemically pure solvents were purified and dried before use by literature method. The ligand used in the present work were not commercially available hence were synthesized in our laboratory. These newly synthesized ligands were characterised by IR, ^{1}H NMR. The following six ligands were synthesized.

1. N- ((3,5,-diphenyl)-4H-1,2,4-triazole-4yl)isonicotinamide. L_1
2. N-(3-(2-hydroxyphenyl)-5(4-nitrophenyl)-4H-1,2,4-triazole -4 yl)isonicotinamide. L_2
3. N-(3-(4-methoxyphenyl)-5-(4-nitrophenyl)-4H-1,2,4-triazole-4yl)isonicotinamide. L_3
4. N- (3,5bis (4-nitrophenyl)-4H-1,2,4-triazole -4 yl) isonicotinamide. L_4
5. N- (3-(phenyl)-5-(4-nitrophenyl 4H-1,2,4-triazole -4yl)isonicotinamide. L_5
6. N- (3-(2 chlorophenyl)-5-(4-nitrophenyl)-4H-1,2,4-triazole-4yl)isonicotinamide.L_6

Synthesis of ligands

The ligands L_1, L_2, L_3 and L_4 were synthesised by literature method [9].

Preparation of L_1, L_2, L_3 and L_4

A mixture of substituted 1,3,4-oxadiazole (0.01 mole) and isoniazid (0.01 mole) in dry pyridine (10ml) was refluxed for 6-8 hr. The reaction mixture was cooled to room temperature

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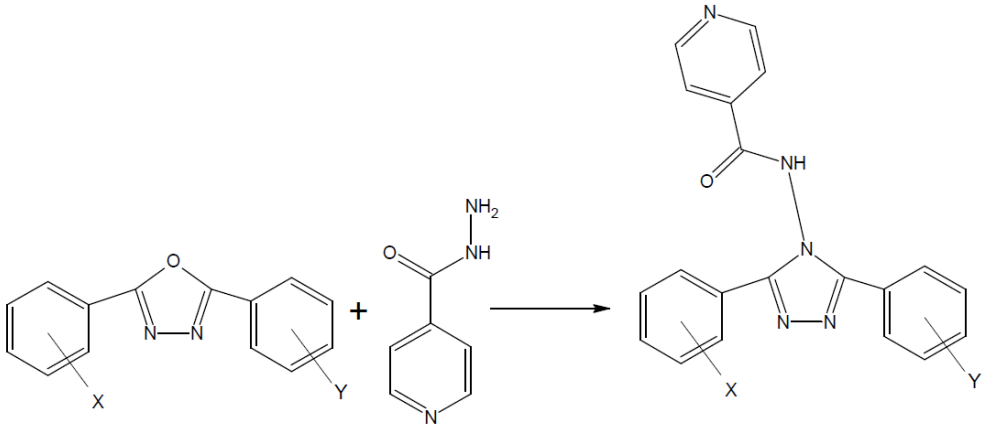
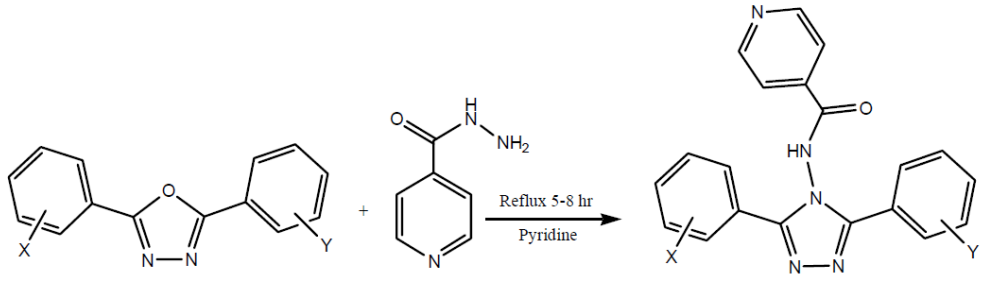
and then the contents were poured on to crushed ice and neutralized with dilute HCl solution. The resulting solid was dried and crystallized from glacial acetic acid. The scheme is as shown in fig.



Compound	X	y
L1	-H	-H
L2	$-NO_2$	-OH
L3	$-NO_2$	-OMe
L4	$-NO_2$	$-NO_2$

Preparation of L_5 and L_6

Also ligands L_5 and L_6 were synthesised by literature method [10] as follows. A mixture of substituted 1,3,4-oxadiazole (0.01 mole) and isoniazid (0.01 mole) in dry pyridine (10ml) was refluxed for 5-8 hr. The reaction mixture was cooled to room temperature and then the contents were poured on to crushed ice and neutralized with dilute HCl solution. The resulting solid was dried and crystallized from glacial acetic acid. The scheme is as shown in fig.



Compound	X	y
L5	4-NO_2	H
L6	4-NO_2	2-Cl

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^{1}H NMR spectra of data of ligands

The value following by the number of protons nature of peak and group cantoning protons in parenthesis are given for each ligand

Ligand (L_1):-N- ((3,5,-diphenyl)-4H-1,2,4-triazole -4 yl) isonicotinamide show the following pick

1. δ 7.3 (s ,1H ,NH)
2. δ .6-7.8(m, 10H, aromatic)
3. δ 8.2 (m, 4H ,hetero-aromatic)

Ligand (L_2):-N- (3-(2-hydroxyphenyl)-5(4-nitrophenyl)-4H-1,2,4-triazole -4 yl) isonicotinamide show the following pick

1. δ 7.32 (s ,1H ,NH)
2. δ 7.1 (m, 8H,aromatic)
3. δ 8.4 – 8.6 (m, 4H ,hetero-aromatic)
4. δ 8.8 (s, 1H ,OH)

Ligand (L_3):- N- (3-(4-methoxyphenyl)-5-(4-nitrophenyl)-4H-1,2,4-triazole -4yl) isonicotinamide show the following pick

1. δ 7.34 (s ,1H ,NH)
2. δ 7.1 (m, 8H, aromatic)
3. δ 8.2-8.6 (m ,4H ,hetero-aromatic)
4. δ 3.9 (s ,3H ,OCH_3)

Ligand (L_4):- N- (3,5bis (4-nitrophenyl)-4H-1,2,4-triazole -4 yl) isonicotinamide show the following pick

1. δ 7.2 (s ,1H ,NH)
2. δ 8.12 (m, 8H, aromatic)
3. δ 8.41-8.6 (m ,4H ,hetero-aromatic)

Ligand (L_5):- N- (3-(phenyl)-5-(4-nitrophen 4H-1,2,4-triazole -4 yl) isonicotinamides how the following pick

1. δ 7.24 (s ,1H ,NH)
2. δ 7.64 (m, 9H, aromatic)
3. δ 8.2-8.8 (m ,4H ,hetero-aromatic)

Ligand (L_6):-N- (3-(2 chlorophenyl) 5-(4-nitrophenyl)-4H-1,2,4-triazole -4 yl) isonicotinamide show the following pick

1. δ 7.25 (s ,1H ,NH)
2. δ 7.82 (m, 8H ,aromatic)
3. δ 8.2-8.6 (m, 4H ,hetero-aromatic)

Synthesis of complexes

Metal salts cupric nitrate (0.01mole) and the ligands (0.02mole) of the dissolved separately in absolute ethanol (25 ml) and DMF–ethanol (1:4 v/v, 25 ml) respectively. Both the solution were filtered and mixed in hot condition. The reaction mixture was refluxed for 4-6hr in a water bath. The coloured product obtained was filtered, washed several times with hot water followed by ethanol and diethyl ether and finally dried over fused calcium chloride.

PHYSICAL MEASUREMENTS

The estimation of carbon, hydrogen and nitrogen were obtained on a Carlo-Erba 1108 C-H-N-analyser at micro analytical unit SAIF, CDRI, Luknow. The IR spectra were recorded in KBr pellets on a Perkin-Elmer-1600 FT-IR spectrophotometer. The reflectance spectra of the complexes were recorded on a Carry-2390 spectrophotometer using $BaSO_4$ as a dilutant and MgO as a reference in the range 200-1500 nm at SAIF, IIT Chennai. ^{1}H-NMR spectrum of the ligand was recorded in a mixed solvent (*$CDCl_3$ + DMSO*) on a bruker AC-200F, 300MHZ, NMR spectrometer using *TMS* as an internal standard at RSIC- Punjab university, Chandigarh. Magnetic measurements were carried out at room temperature using Gouy's method using Hg [Co (SCN)$_4$] as calibrant and values were corrected for diamagnetism by using Pascal's constant. Thermogravimetric analyses of the complexes were carried out using a TGS-2Perkin Elmer thermal analyzer in the temperature range 50-700 ^oC at a heating rate of 10 ^oC min^{-1}. Antibacterial and antifungal activities of the ligand and their complexes were carried out against the bacteria *E. coli and S. aureus* by cup plate method.

RESULTS AND DISCUSSION

The required 1,3,4-oxadiazoles prepared by refluxing a mixture of substituted benzohydrazide and substituted benzoic acid in phosphorus oxychloride for 4-6 hours. Then these oxadiazolesm were refluxed with isoniazide in dry pyridine. The ligands were confirmed on the basis of IR, NMR and nitrogen analysis. The physical characterization and micro analytical data of ligands and its coordination complexes are given in (Table 1). All the complexes are coloured solids, air stable and are having line solubility in polar solvents DMF and DMSO. The elemental analyses shown in Table 1 indicate that all these complexes have 1:2 metal: ligand stoichiometry and were in good agreement with the values calculated from proposed formula.

IR Spectra

The IR spectra of the ligand were recorded for the identification of their donor sites in frequencies after their complexation with metal ion. The Partial listing of the IR spectra of the ligand is given in Table 2 the entire ligand exhibit following assignment.

1. A medium sharp absorption band around at 3290-3180 cm^{-1} is assigned to N-H stretching vibration of NH group of the ligands.[11]
2. A strong absorption band at 1685-1665 cm^{-1} is due to C=O (amide) stretching frequency [12, 13]
3. A strong absorption band at 1617-1603 cm^{-1} is assigned to C=N (imine) starching vibration [12, 13].
4. A medium band at 1535-1480 cm^{-1} may be assigned to C-O phenolic stretching vibration [14-16].
5. A weak band appearing at 1070-1060 cm^{-1} is attributed to pyridine ring breathing vibration [17].
6. A weak band at 1000-990 $cm^{-1}$is assigned to N-N stretching vibration [17].

Electronic spectra and magnetic studies

The magnetic moments for Cu (II) complexes are given in Table 1. at room temperature corresponding to one unpaired electron. The electronic spectrum of Cu (II) complex displayed band at 16478-16562cm^{-1} as signed for the $^{2}T2_{g} \rightarrow {}^{2}E_{g}$ transition. The electronic transitions and magnetic moment value suggests pseudo octahedral geometry around Cu (II) ion [18-20]. A detailed interpretation of the electronic spectra of Cu (II) complexes is rather complicated owing to distorted octahedral which is very common in Cu (II) complexes which give strong charge transfer bands telling off in the blue end of the visible spectrum.

Thermogravimetric analysis

In the present investigation, analysis of TG curves of ligands and its Cu complexes reveals a two stage decomposition pattern. All the Cu complexes are almost stable upto 70-80^{o}C. The Cu complexes loss their weight in the range 180-230 ^{0}C corresponding to two coordinated water molecules. The Cu (II) complexes show a gradual but continuous weight loss between 265-645^{o}C due to oxidative thermal degradation of ligand. The final stage ends with the arial oxidation of the complexes and formation of respective stable metal oxide. The thermal decomposition temperature is as shown in Table 1.

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Table 1:The Proposed composition, formula weight, colour, Thermal data and Magnetic moment of Ligands and its Cu(II) Complexes

Sr.no	Ligand	M.P./ Half Decomp Temp ^{0}C	Yield (%)	Molecular Formula	Formula Weight	Colour	C%	H%	N%	M %	Magnetic Moment in B.M.
1.	L_1	148	65	$C_{20}H_{15}N_5O$	341.366	Creamish	69.22 (70.00)	4.48 (4.39)	21.36 (20.50)	--	--
2.	L_2	218	60	$C_{20}H_{14}N_6O_4$	402.363	Pale yellow	58.26 (59.64)	3.49 (3.47)	19.98 (20.87)	--	--
3.	L_3	235	58	$C_{21}H_{16}N_6O_4$	416.390	Yellow	61.38 (60.52)	3.96 (3.84)	20.79 (20.17)	--	--
4.	L_4	232	62	$C_{20}H_{13}N_7O_5$	413.361	Pale yellow	58.02 (58.06)	4.12 (3.14)	24.06 (23.70)	--	--
5.	L_5	178	68	$C_{20}H_{14}N_6O_3$	386.364	Yellow	62.48 (62.11)	3.79 (3.62)	22.58 (21.74)	--	--
6.	L_6	187	56	$C_{20}H_{13}ClN_6O_3$	420.809	Yellow	58.25 (57.03)	4.25 (3.08)	20.36 (19.96)	--	--
7.	Cu L_1Complex	378	58	$Cu[C_{40}H_{32}N_{10}O4]$	779.16	Blue	61.23 (61.57)	4.12 (4.13)	18.25 (17.95)	7.75 (8.14)	1.89
8.	Cu L_2Complex	392	62	$Cu[C_{40}H_{30}N_{12}O_{10}]$	901	Green	53.55 (53.25)	3.05 (3.35)	18.26 (18.33)	7.52 (7.04)	1.86
9.	Cu L_3Complex	400	54	$Cu[C_{42}H_{34}N_{12}O_{10}]$	930.34	Green	54.93 (54.22)	3.64 (3.68)	18.25 (18.07)	6.68 (6.83)	1.81
10.	Cu L_4Complex	294	64	$Cu[C_{40}H_{38}N_{14}O_{12}]$	1018.2	Green	51.26 (51.89)	3.86 (3.76)	20.06 (19.25)	6.89 (6.24)	1.92
11.	Cu L_5Complex	320	69	$Cu[C_{40}H_{40}N_{12}O_8]$	928	Green	56.76 (56.92)	3.99 (4.34)	18.02 (18.10)	7.06 (6.84)	1.85
12.	Cu L_6Complex	340	63	$Cu[C_{40}H_{38}Cl2N_{12}O_8]$	939	Green	51.95 (51.15)	3.05 (3.01)	17.26 (17.90)	7.01 (6.77)	1.96

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Antimicrobial Activity

The antibacterial screening of ligands and its Cu-complexes reveals that the free ligand shows moderate activity against all bacterial strains [21, 22] as shown in Table 3. Cu(II)-L_4 complexes show maximum activity against *E. Coli* (gram positive) bacteria, Cu(II)-L_2, Cu(II)-L_5 complexes show maximum activity against *S. aureus* bacteria whereas, Cu(II)-L_1 Cu(II)-L_3, Cu(II)-L_6 show moderate activity against *S. aureus.* The antibacterial data reveals that the Cu complexes are more bioactive than the free ligand.

Table 2: IR Spectral data (cm^{-1}) of the Ligands and Cu(II) metal complexes.

S.no	Ligand	ν (N-H)	ν (C=O)	ν (C=N)	ν (M-N)	ν (H_2O)	ν (C-O)
1.	L_1	3245	1729	1615	--	--	1230
2.	L_2	3201	1727	1589	--	--	1312
3.	L_3	3209	1732	1576	--	--	1305
4.	L_4	3218	1735	1577	--	--	1292
5.	L_5	3245	1731	1575	--	--	1299
6.	L_6	3210	1728	1579	--	--	1300
7.	Cu L_1Complex	--	--	1556	425	3360,789	1301
8.	Cu L_2Complex	--	--	1588	436	3446,860	1295
9.	Cu L_3Complex	--	--	1578	466	3376,834	1292
10.	Cu L_4Complex	--	--	1566	467	3387,898	1296
11.	Cu L_5Complex	--	--	1520	456	3380,882	1276
12.	Cu L_6Complex	--	--	1556	458	3290,898	1290

Table 3: Antimicrobial activity of the Ligands and Cu(II) metal complexes.

S No.	Compound	Antimicrobial Activity of zone of inhibition (in mm)	
		E.coli	*S.aureus*
1	L_1	15	14
2.	L_2	18	19
3.	L_3	16	19
4.	L_4	15	15
5.	L_5	16	17
6.	L_6	16	18
7.	Cu L_1Complex	19	18
8.	Cu L_2Complex	15	21
9.	Cu L_3Complex	18	19
10.	Cu L_4Complex	21	17
11.	Cu L_5Complex	16	22
12	Cu L_6Complex	19	16

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