

Microwave Irradiative Synthesis, Characterization and Evaluation of Antimicrobial Activity of Co(II), Ni(II) and Cu(II) complexes with ligands 2-(2-hydroxy benzylidene amino)-4-benzylidene amino-6-methyl-1, 3, 5-triazine derivatives

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ABSTRACT: Complexes of Co(II), Ni(II) and Cu(II) with 2-(2-hydroxy benzylidene amino)-4-benzylidene amino-6-methyl-1, 3, 5-triazine [HL¹] and 2-(2-hydroxy-5-chloro benzylidene amino)-4-benzylidene amino-6-methyl-1, 3, 5-triazine [HL²] have been prepared. Elemental, conductance, magnetic moment, infrared, NMR, ESR, and electronic spectral studies have characterized these complexes. Stoichiometry (1:1) ML was found in the complexes. Square pyramidal geometry has been assigned to these complexes based on spectral and magnetic studies. For antimicrobial activity, the prepared ligands [HL¹] and [HL²] and their cobalt(II), nickel(II) and copper(II) complexes have been carried out. Compared to the ligands and other metal complexes, all the copper complexes Cu(L¹)H₂O and Cu(L²)H₂O were found to be most active against all the microbes examined.

Keywords: Triazines, Metal complexes, Magnetic moment, Electronic spectra, stoichiometry.

I. INTRODUCTION

A symmetrical triazine is a six-membered heterocyclic compound containing of three carbon atoms and three nitrogen atoms alternatively placed in the ring. Symmetrical triazine (1, 3, 5-or γ -triazine) is abbreviated as S-triazine. The asymmetrical triazines are abbreviated as as-triazines. They are 1, 2, 4 or α -triazine and 1, 2, 3 or β triazine[1]. The aza derivatives of benzene is a six membered conjugated rings which consist of one or more nitrogen atoms in the ring. Increasing the number of nitrogen atom on the ring leads to electron density withdrawal from the carbon atoms that results in lowering of the energies of the π -molecular orbitals. Such aromatic heterocyclic compounds are often known as π -deficient

heterocyclic compounds. This phenomenon rises the difficulty of electrophilic attack on the ring carbon atoms but nucleophilic attack become easier[2]. S-triazine (1,3,5-triazine) is quite stable, aromatic in character and susceptible to nucleophilic attack. It rapidly decomposes in water[3]. For the synthesis of different derivatives, S-triazine is not usually used as the starting material due to its high reactivity. A 2,4,6-trichloro-s-triazine (cyanuric chloride) is one of the predominant form from which other derivatives are synthesized. It exists as white crystals and has a pungent odour[4]. Chemical substances that are formed by the linkage of metallic species with electron donating ligands are termed as metal complexes. Because of improved electron density distribution and solubility, those that are derived from biologically active organic compounds have important applications. The coordinating centers and structures of the metal complexes play a vital role in almost all biological activities. It is reasonable to expect suppression or enhancement of herbicide activity when active heterocyclic centers are bound to metal ions[5]. The electrons in the S-triazine ring are positioned in the vicinity of the nitrogen centers because of the difference in electronegativity between nitrogen and carbon, enabling metal ion coordination. [6]. the literature survey also shows the increasing interest of preparation of substituted S-triazine, elucidation of structure and applications of transition and non transition metal complexes. Ca²⁺, Sr²⁺ and Ba²⁺ complexes with tri mercaptotriazine, and those with 2, 4, 6-tris-(2-pyridyl)-1, 3, 5-triazine, Pb²⁺, Ni²⁺, Cu²⁺, and Co²⁺ have been recorded [7]. Various synthetic routes are there for synthesizing multi dentate triazine ligands and their metal complexes

The present research focuses on the preparation, physic-chemical characterization and evaluation of antimicrobial studies of cobalt(II), nickel(II) and copper(II) complexes of certain ligands such as 2-(2-hydroxy benzylidene amino) -4-benzylidene amino-6-methyl- 1, 3, 5-triazine [HL¹] and 2-(2-hydroxy-5-chloro benzylidene amino) -4-benzylidene amino-6-methyl-1, 3, 5-triazine [HL²]

II. MATERIALS AND METHODS

All chemicals used are analytical grade was used in the present investigation. To estimate the metal content, normal gravimetric methods were used; cobalt was calculated to be cobalt as cobalt oxanate, nickel as nickel dimethyl glyoximate and copper as copper salicylaldoxime [10].

INSTRUMENTATION

In the Perfit electric melting point apparatus, melting points in open capillaries have been measured and are inaccurate. Using the Perkin-Elmer 2400 Elemental Analyzer, carbon , hydrogen and nitrogen were estimated at central university, Hyderabad. From the micro study of the metal complexes data indicate that the hydration water in complexes. Electronic spectra of metal

complexes were reported in DMF by using Hitachi U-2000 spectrophotometer in the 1100-200 nm range. In the 4000-250 cm⁻¹ range, the Beckman IR-20 Spectrophotometer reported IR spectra in KBr / Nujol mulls. For proton NMR spectra Bruker ACF 300 spectrometer at 300 MHz. was used, 'tetramethylsilane' as the internal standard in DMSO-d₆. Magnetic moments of the samples were measured on a vibrating magnetometer at IIC, IIT Roorkee (Model 155).

Microwave Irradiated Synthesis of 2-amino-4-benzylidene amino-6-methyl -[1, 3, 5]-triazine:

The 2-amino-4-benzylidene amino-6-methyl-[1,3,5]-triazine compound was prepared for 3.5 minutes under solvent-free conditions by microwave irradiation of 2,4-diamino-6-methyl-[1,3,5]-triazine (0.02 mol) and benzaldehyde (0.02 mol).. Hot ethanol (95%), m.p.143⁰C (Found: C, 62.0; H, 5.12; N, 32.90. Calcd. For C₁₁H₁₁N₅: C,61.97; H, 5.16; N,32.86 percent);¹H NMR: (CDCl₃ + DMSO-d₆) 7.94 (1H, s, Ar-CH = N),7.90 (2H, s, Trz-NH₂), 6.90-7.58 (5H), m, Ar-H),2.27 (3H, s, Trz-CH₃)[11, 12].58 (5H), 2.27 (3H, s TLC controlled the preparation of the compound using silica gel-G plates and the pure compound was extracted using the column chromatography technique.

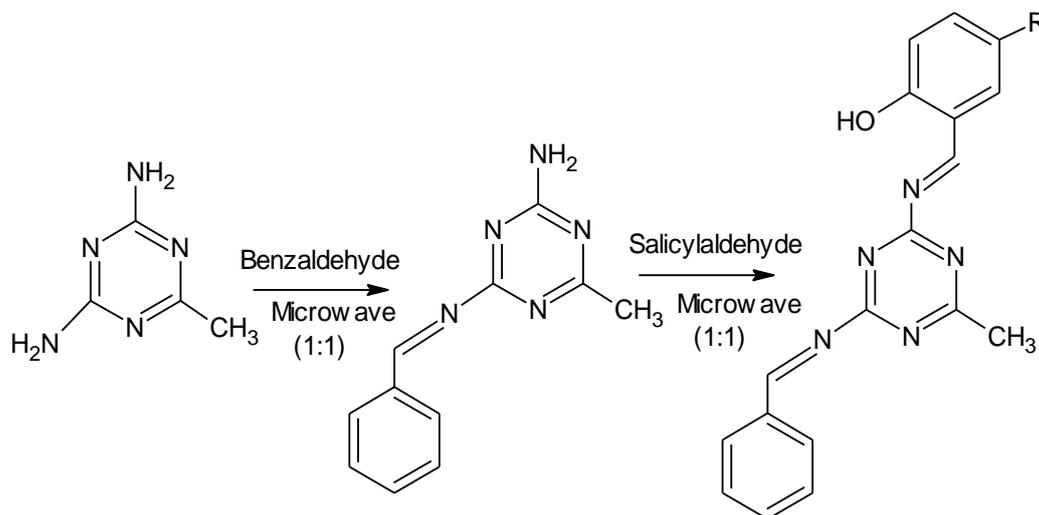


Fig.1. Triazine derivatives Schiff base ligands

2-(2-hydroxy benzylidene amino) -4-benzylidene amino-6-methyl-[1, 3, 5]-triazine [HL¹] and **2-(2-hydroxy-5-chloro benzylidene amino) -4-benzylidene amino-6-methyl-[1, 3, 5]-triazine[HL²]:**

The crude solid mass obtained was crystallised from hot ethanol by treating [0.02 mol] with

substituted salicyl aldehyde (0.02 mol.) for 3 minutes during microwave irradiation.

Microwave Irradiated Synthesis of cobalt(II), nickel(II) and copper(II) complexes with ligands [HL¹] and [HL²]

Hot solution 2-(2-hydroxy-benzylidene amino)-4-benzylidene amino-6-methyl-[1, 3, 5]-

triazine (HL¹) / 2-(2-hydroxy-5-chloro benzylidene amino)-4-benzylideneamino-6-methyl-[1,3,5]-triazine (HL²) (0.001mol) in ethanol was incorporated to the hot solution of metal salts; the reaction mixture was refluxed in microwave irradiation for 3 to 4 minutes. The solid complexes were separated as crude allowed to settle and accumulate, then filtered washed with distilled water and then with hot ethanol. The obtained solid

complexes were dried in desiccators over anhydrous calcium chloride.

The ready ligands [HL¹] and [HL²] and their cobalt(II), nickel(II) and copper(II) complexes were screened using the cup plate method for their antibacterial and antifungal activity. Minimum inhibitory concentration (MIC) approaches at different concentrations of DMSO solvent were used to conduct antibacterial and antifungal activities.

Table-1. Analytical data of metal complexes with 2-(2-hydroxy benzylidene amino) -4-benzy lideneamino-6-methyl-[1, 3, 5]-triazine [HL¹] and 2-(2-hydroxy-5-chloro benzylidene amino) -4-benzylidene amino-6-methyl-[1, 3, 5]-triazine [HL²]:

Ligands / Complexes	C	H	N	M	Cl	Molar conductance (Scm ² mol ⁻¹)	Magnetic Moment μ_{eff} (BM)
HL ¹	62.00 (61.97)	5.22 (5.16)	32.74 (32.86)	--	-	--	--
HL ²	64.25 (64.19)	4.50 (4.45)	20.85 (20.80)	--	10.61 (10.53)	--	--
Co(L ¹)H ₂ O	42.92 (42.87)	4.80 (4.87)	22.76 (22.73)	19.05 (19.13)	-	103.5	3.15
Ni(L ¹)H ₂ O	42.95 (42.90)	4.82 (4.87)	22.69 (22.75)	19.00 (19.07)	-	106.4	2.85
Cu(L ¹)H ₂ O	42.18 (42.23)	4.85 (4.79)	22.42 (22.39)	20.36 (20.33)	-	112.3	1.73
Co(L ²)H ₂ O	50.00 (50.07)	4.38 (4.40)	16.65 (16.62)	13.70 (13.66)	8.25 (8.21)	108.3	3.12
Ni(L ²)H ₂ O	50.14 (50.09)	4.35 (4.40)	16.25 (16.23)	13.57 (13.61)	8.25 (8.22)	105.7	2.83
Cu(L ²)H ₂ O	53.90 (53.86)	4.80 (4.73)	17.50 (17.45)	15.85 (15.84)	8.80 (8.84)	115.3	1.74

*The values in the parenthesis were calculated one

III. RESULT AND DISCUSSION

All the investigated complexes were stable at room temperature and coloured, these complexes are soluble in common organic solvents In Table-1, analytical and molar conductance data is given for ligands and their complexes. The molar conductance data in DMF solution for all investigated complexes were within the 103-115 ohm⁻¹ cm² mol⁻¹ range, which is the complexes 1:1 electrolytic[13] characteristic.

In DMF, the UV-Vis spectrum of complexes was reported and characterized by multiple spectral regions. The absorption bands of the ligands are attributable to the n → π* & π → π* transitions[14,15] in the area of 26525 cm⁻¹ and 37037 cm⁻¹. In the copper(II) complexes electronic spectrum, two absorption bands around 16918 cm⁻¹ and 19878 cm⁻¹ are present, which are assigned to

transitions ²B₁ to ²A₁ (v₁) and ²B₁ to ²E_g (v₂) for square pyramidal geometry[16]. The electronic spectra of the nickel(II) complexes, the absorption bands at 10132 cm⁻¹, 13017 cm⁻¹ and 17605 cm⁻¹ were due to the transitions from ³B₁(F) → ³E(F), ³B₁(F) → ³A₂(P) and ³B₁(F) → ³E_g(P) respectively, which suggests that the nickel(II) complexes were having five-coordinate square pyramidal geometry[17]. Absorption bands at 11750 cm⁻¹ and 17650 cm⁻¹ for the cobalt(II) complexes can be assigned to transitions of ⁴A₂→⁴B₁ and ⁴A₂→⁴E_g(P) which suggests that the square pyramidal geometry, respectively[18]. The magnetic moment of the Cu(II) complex, also confirmed the five coordinate square pyramidal geometry, is 1.74BM (Table-1)[19]. The square pyramidal geometry is further confirmed by the cobalt(II) and nickel(II)

complexes with magnetic moment values of 3.11 BM and 2.84 BM, respectively[20].

For ligands and their complexes, the infra red spectral frequencies (cm^{-1}) were analyzed. The IR spectrum of free ligands shows in the range $3265\text{-}3279\text{ cm}^{-1}$ due to $\nu_{\text{(OH)}}$ intra molecular bonding. Stretching modes $\nu_{\text{C=N}}$ (azomethine), $\nu_{\text{C=C}}$ (Aromatic double bond) and $\nu_{\text{C-N}}$ (aryl azomethine) groups around 1600 cm^{-1} , 1662 cm^{-1} and 1232 cm^{-1} are assigned respectively. In the case of complexes, shifts and splits suggesting s-triazine nitrogen participation in coordination are shown by absorption bands that appeared around 1587 cm^{-1} corresponding to the $\nu_{\text{C=N}}$ stretching vibrations of triazine rings of the ligands[21]. The weak bands can be observed at $400\text{-}430\text{ cm}^{-1}$ and 587 cm^{-1} regions due to $\nu_{\text{M-N}}$ and $\nu_{\text{M-O}}$ vibrations[22] respectively in complexes, validate the association between the metal ions bonding with the ligands [22]. The high frequency bands $3200\text{-}3600\text{ cm}^{-1}$ in the range of the infra red spectrum due to stretching modes of ordered water molecules..

For ligands $[\text{HL}^1]$ and $[\text{HL}^2]$ and their metal complexes, ^1H NMR spectral data have been reported based on literature data. [23]. In the NMR spectrum of complexes, we have detected a shift in electron density from the ligands to the metal. The ligands $[\text{HL}^1]$ and $[\text{HL}^2]$ display a signal at δ 8.7-8.8 and 2.2-2.4 ppm respectively. This is assigned to azomethine proton attached to azomethine carbon and methyl group protons attached to the triazine ring, respectively. These signals seen in the metal complex spectrum imply the involvement of the metal ion with azomethine nitrogen atom of the ligands. In addition to this, phenolic OH

protons are ascribed to the signals at δ 11.5 and 11.8ppm. The absence of these OH proton signals in the metal complexes spectra helped the phenolic OH group of deprotonation. Multiple signals about δ 7.3–8.1 and δ 6.4–7.7 ppm were allocated to aromatic protons in the spectrum of ligands. Such various differences suggest a minor change in coordination.

Based on analytical data, electronic spectra, magnetic susceptibility and conductance measurements, IR, NMR spectral data, were assigned the square pyramidal geometry for all metal complexes.

The prepared ligands $[\text{HL}^1]$ and $[\text{HL}^2]$ and their cobalt(II), nickel(II) and copper(II) complexes have been evaluated for antimicrobial activity and their results are given in table-2 [24]. Antibacterial study was carried out using *Shigella flexneri* and *Enterococcus* and antifungal activity using *Candida parasilopsis* and *Malassesia pachydermatis*. Standard drugs Ampicillin and Nystatin were also tested at the same concentration for their antibacterial and antifungal study in similar conditions[25].

The findings indicate that, relative to their ligands, all metal complexes were revealed superior bacterial and fungal activities. In contrast to their ligands, all the copper complexes $\text{Cu}(\text{L}^1)\text{H}_2\text{O}$ and $\text{Cu}(\text{L}^2)\text{H}_2\text{O}$ were found to be most active against all the microbes studied, because of the faster dissemination of the copper(II) complexes Whereas, the complexes Ni(II) and Co(II) have demonstrated mild activity[26]. Both metal complexes, however, have increased antimicrobial activity compared to the $[\text{HL}^1]$ and $[\text{HL}^2]$ ligands.

Table-2. The antimicrobial activities of the ligands $[\text{HL}^1]$ and $[\text{HL}^2]$ and their cobalt(II), nickel(II) and copper(II) complexes are measured in (mm).

Ligands/ complexes	Zone of inhibition in mm			
	Antibacterial activity		Antifungal activity	
	Shigella flexneri	Enterococcus	Candida parasilopsis	Malassesia pachydermatis
$[\text{HL}^1]$	15	14	18	14
$[\text{HL}^2]$	16	16	16	16
$\text{Co}(\text{L}^1)\text{H}_2\text{O}$	22	18	24	23
$\text{Ni}(\text{L}^1)\text{H}_2\text{O}$	24	24	26	26
$\text{Cu}(\text{L}^1)\text{H}_2\text{O}$	29	28	36	29
$\text{Co}(\text{L}^2)\text{H}_2\text{O}$	16	18	26	22
$\text{Ni}(\text{L}^2)\text{H}_2\text{O}$	15	19	27	24
$\text{Cu}(\text{L}^2)\text{H}_2\text{O}$	32	29	35	30
Ampicillin	36	32	--	--
Nystatin	--	--	42	34

IV. CONCLUSION

The preparation and characterization of new tetradentate ligands has been published in this paper, namely: 2-(2-hydroxy benzylidene amino)-4-benzylidene amino-6-methyl-[1,3,5]-triazine[HL¹] and 2-(2-hydroxy-5-chloro benzylidene amino)-4-benzylidene amino-6-methyl-[1,3,5]-triazine[HL²] and their cobalt(II), nickel(II) and copper(II) complexes. All complexes are coloured, air-stable and insoluble in water and common solvents, but soluble in polar solvents such as DMF and DMSO. 1:1(M: L) stoichiometry for all complexes was suggested by the analytical data obtained. There is an electrolytic nature of the prepared complexes. On the basis of analytical IR, electronic spectral data, ¹H NMR spectra, magnetic, conductance measurements, the square pyramid geometry for all metal complexes was proposed. The ligands [HL¹] and [HL²] and their cobalt(II), nickel(II) and copper(II) complexes were examined for antimicrobial activity. It was found that, as compared to their ligands, all copper complexes (Cu(L¹)H₂O and Cu(L²)H₂O) were observed most active against all the microbes tested, due to the faster penetration of the Cu(II) complexes through the cell membrane of microbes.

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REFERENCES

- [1]. Elderfield R.C., 1961, Heterocyclic Compounds; first edition, John Wiley and sons, London, 7.
- [2]. Gilchrist T.L., 1992, Heterocyclic Chemistry, 2nd edition, John Willey and Sons, London, 298.
- [3]. Joule J.A. and Smith G.F., 1978, Heterocyclic Chemistry; 2nd edition. 125.
- [4]. Young D. W. Heterocyclic Chemistry; 1975, Longman, London and New York, 1-3.
- [5]. DejeneDisasaIrga, Raju V.J.T, 2016, Template synthesis and characterization of Ni(ii) complex derived from 4phenoxy-2,6-dichloro-s-traizine and 2,4-dinitrophenylhydrazine. International Journal of Advanced Research, 4, 6, 873-886.
- [6]. Smolin E. and Rapport L., 1959, Chemistry of Heterocyclic Compounds; Wiley Interscience, New York, 13, 293-301.
- [7]. Worku Assefa., 2004, Synthesis and Characterization of Transition metal complexes derived from a new Nitrogen Heterocyclic Chelating system and study on the possible Application; M.Sc. Thesis.
- [8]. A. I.Vogel, 1999, A Text book Qualitative Chemical Analysis, 5thedn. , Addison Wesley Longman, London.
- [9]. N.B. Colthup, L.H. Dally and S.E. Wiberly, 1964, Introduction to Infrared and Raman Spectroscopy, Academic Press: New York. 18.
- [10]. R.M. Silverstein, G.C. Bassler and T.C. Morrill, 1981, Spectrometric Identification of Organic Compounds, John Wiley & Sons: New York, Edn.4.
- [11]. Kiran Singh, Yogender Kumar and Manjeet S. Barwa, 2010, Synthesis, Characterization and Thermal Studies of Co(II), Ni(II), Cu(II) and Zn(II) Complexes of Some Schiff Bases Derived from 4-Amino-3-mercapto-6-methyl-5-oxo-1,2,4-triazine., S. Afr. J. Chem., 63, 169-174.
- [12]. Parimal Paul, 2002, Ruthenium, osmium and rhodium complexes of polypyridyl ligands: Metal-promoted activities, stereochemical aspects and electrochemical properties., Proc. Indian Acad. Sci. (Chem. Sci.), 114, 4, 269-276.
- [13]. Dani Peri, Jacob S. Alexander, Edit Y, Tshuva and Artem Melman, 2006, Distinctive structural features of hydroxyamino-1, 3, 5-triazine ligands leading to enhanced hydrolytic stability of their titanium complexes., Dalton Trans., 4169-4172
- [14]. A. B. P. Lever, 1984, Inorganic Electronic Spectroscopy, 2nd Edition, Elsevier, Amsterdam, Oxford New York.
- [15]. D. N. Sathyanarayana, 2001, Electronic Absorption Spectroscopy and Related Techniques, Universities Press.
- [16]. Mohammed, R., Chastanet, G., Tuna, F., Malkin, T. L.; Barrett, S. A., Kilner, C. A.
- [17]. Létard, J.-F. Halcrow, M. A. 2013, The Synthesis of New 2,6-Di(pyrazol-1-yl)pyrazine Derivatives, and the Spin State Behavior of their Iron(II) Complexes. Eur. J. Inorg. Chem. 819-831.
- [18]. Halcrow, M. A. 2009, Iron(II) Complexes of 2,6-Di(pyrazol-1-yl)pyridines – a Versatile

- System for Spin-Crossover Research. *Coord. Chem. Rev.* 253, 2493–2514.
- [19]. Gamez, P. Reedijk, J., 2006, 1,3,5-Triazine-Based Synthons in Supramolecular Chemistry. *Eur. J. Inorg. Chem.* 2006, 29–42.
- [20]. Safin, D. A.; Frost, J. M.; Murugesu, M., 2015, The Renaissance of 2,4,6-Tris(2-pyrimidyl)-1,3,5-triazine (TPymT) Coordination Chemistry. *Dalton Trans.* 44, 20287–20294.
- [21]. Halcrow, M. A. (ed), 2013, Spin-Crossover Materials - Properties and Applications, John Wiley & Sons, Ltd.: New York, p. 568.
- [22]. Ohtani, R. Hayami, S., 2017, Guest-Dependent Spin-Transition Behavior of Porous Coordination Polymers. *Chem. Eur. J.* 23, 2236–2248.
- [23]. F. C. Odds, 1989, Antifungal activity of saperconazole (R 66 905) in vitro. *Journal of Antimicrobial Chemotherapy*, 24, 533.
- [24]. Butler RN, Fahy A M, 2006, New reactive fluorophores in the 1,2,3-triazine series. *Tetrahedron Letters*, 47, 1721-4.
- [25]. Bacchi CJ, Vargas M, Rattendi D, Goldberg B, Zhou W, 1998, Antitrypanosomal Activity of a New Triazine Derivative, SIPI 1029, In vitro and in model infections. *antimicrobial agents and chemotherapy*, 42(10), 2718–2721.