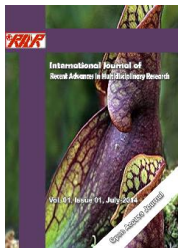

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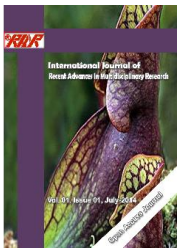

Research Article

SYNTHESIS AND CHARACTERIZATION WITH ANTIBACTERIAL, ANTIFUNGAL, CYTOTOXICITY STUDIES ON THE CO (II), NI (II) AND CU (II) COMPLEXES OF TRIDENTATE ONO COORDINATING SCHIFF BASES AND HETEROCYCLIC AMINES

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ABSTRACT

Some Schiff base complexes of Co (II), Ni (II) and Cu (II) containing heterocyclic amines has been prepared. The complexes were isolated from the reaction in solid forms and characterized by IR, ^{1}H NMR, UV- Vis., and some physical measurements. The observed values confirmed that the complexes have tetrahedral/square planar geometry. The complexes have been found to have moderate to strong antimicrobial, antifungal and cytotoxic activity.

INTRODUCTION

The Schiff base ligands are derived by the condensation of an active carbonyl group and a primary amine and contain the azomethine group (=C=N-). These bases can be effective chelating agents either the carbonyl compound as the amine or both contain potentially coordinating functional groups near the site of condensation. Schiff base constitute a very important group of N,O donor chelating ligands (Yan-Wen Lin and Yi-Ping Tong 2009, Madhumita Chatterjee *et al*., 1998, Holm R. H. and Connor M. J. O 1971, Abdul Wajid and Rahul B. Mohod 2013 and Halve A. and Goyal A 1996). Schiff bases and their metal complexes are well known to have pronounced biological activities [13-17] and form an important class of compounds in medicinal and pharmaceutical field and azomethine linkage might be responsible for the biological activities of the Schiff bases. A number of complexes containing NNS, ONS and ONN donor sequence have been studied in our laboratory (Tarafder M.T.H *et al*., 1978, M.Al-Amin *et al*., 2011, M.B.H.Howlader *et al*., 2009). However; nothing seems to have been done so far on complexation of ligands having ONN and ONO donor sequence.

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These kinds of ligands provide intriguing chemistry with both lighter and heavier transition metals. Keeping these facts in view we here in report the preparation and characterization of the metal complexes of Co (II), Ni (II) and Cu (II) with tridentate ONO donor schiff bases and heterocyclic amines. Then, we have tried to evaluate their biological activity such as antibacterial, antifungal and cytotoxic properties.

Experimental

Reagents and Chemicals

All the reagents used were of analar or chemically pure grade. Solvents were purified and dried according to standard procedures.

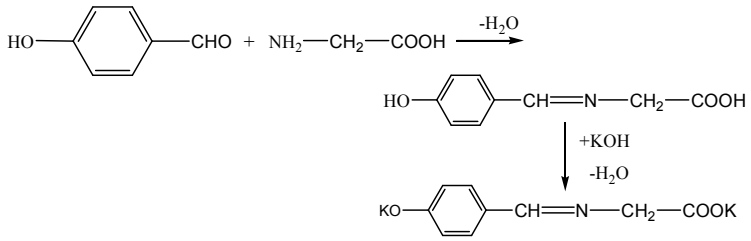
Physical Measurements

The melting or decomposition temperatures of all the prepared metal complexes were observed in an electro thermal melting point apparatus model No.AZ6512. The SHERWOOD SCIENTIFIC Magnetic Susceptibility Balance was used for the present investigation. Infrared spectra as KBr disc were recorded in a SIMADZU FTIR-8400 (Japan) infrared spectrophotometer, from 4000-400 cm^{-1}. The absorbances of the complexes were recorded on SHIMUDZU Spectrophotometer.

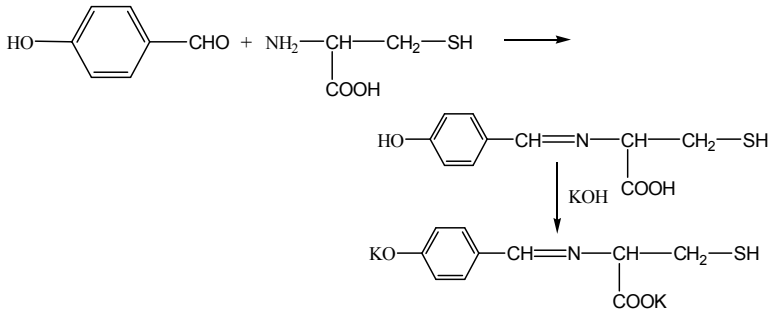
Preparation

General method of preparation of tridentate Schiff bases

P-hydroxybenzaldehyde (4.8848g, 0.04mole) dissolved in absolute ethanol/(20ml)was added slowly with constant stirring to a solution of glycine/L (+) cystine(0.04mole) in water in the presence of potassium hydroxide . The solution was refluxed for 4-5 hrs. The liquid Schiff base was prepared by the distillation process.



Potassium salt of (4-hydroxy-benzylidene)-carbamic acid, Schiff base for glycine (SB-A_1)



Potassium salt of 2-[(4-hydroxy-benzylidene)-amino]-3-mercapto-propionic acid, Schiff base for L(+) cystine (SB-A_2)

Preparation Procedures of (SB-A_1)/(SB-A_2)complexes:

The complexes have the general formula [M(SB)L]; where, M=Ni(II),Co(II), Cu(II), L=Heterocyclic amine [Quinoline , Pyridine, Iso-quinoline ,2-Picoline and 4- Picoline]. SB=Schiff base ligands such as (SB-A_1)/ (SB-A_2)

In a typical preparation 0.002mole of metal salts and 0.002mole of (SB-A_1)/ (SB-A_2) were separately dissolved in minimum amount of absolute alcohol and then the solution were mixed together and heated on water both for an hour. Then an ethanolic solution of L, 0.002 mole was added to the above solution .The resultant mixture was heated under reflux on a water bath for 2 hrs and then cooled .The colored precipitate so formed, was filtered, washed with hot ethanol and dried in a vacuum desiccator over anhydrous $CaCl_2$.

RESULTS AND DISCUSSION

Physical Properties

Some physical properties viz., color melting point, magnetic moments and conductance values are given in Table1. The complexes were soluble in water, N, N'–dimethyl formamide and dimethyl sulfoxide. The conductance values of the complexes in DMSO indicated that the complexes were non-electrolyte in nature.

The values of magnetic moment in Bohr Magneton of the complexes are in good agreement with their respective structures.

Electronic Spectra

The electronic spectra of Co (II) complexes in DMSO gave bands corresponding to the transitions $^4T_{2g}\rightarrow{}^4T_{1g}$, $^4T_{2g}\rightarrow{}^4A_{2g}$ and charge transfer respectively, which are in good agreement with the tetrahedral structure.

The electronic spectra of Ni (II) complexes gave three bands corresponding to the transitions $^1A_{1g}\rightarrow{}^1B_{1u}$, $^1A_{2g}\rightarrow{}^1A_{2u}$ and $^1A_{1g}\rightarrow{}^1E_u$ respectively. Cu (II) complexes in DMSO gave the three bands to the transitions $^2B_{1g}\rightarrow{}^2A_{1g}$, $^2B_{1g}\rightarrow{}^2E_g$ and charge transfer are obtained. These bands of Ni (II) and Cu (II) complexes are consistent with square planar geometry Table 2.

IR Studies

The strong band at (1633-1604) $cm^{-1}$is due to the (C=N) group and other two bands at (1400-1500) cm^{-1} and (1200-1300) cm^{-1} for the asymmetric and symmetric stretching vibration of (-COO) group respectively. These values are somewhat lower than the free ligand indicating the coordination with the metal atoms. Two distinct bands at (510-530) cm^{-1} and (390-490) cm^{-1} for the stretching vibrations of (M-O) and (M-N) bands indicated the complexation of (C-O) and (C=N) group respectively. From the above observation it may be concluded that Schiff base ligand behaves as tridentate dinagative ligand and donates Table 3. On the basis of the elemental analysis, conductivity measurements, magnetic moment data, spectroscopic studies and literature review the possible structure of the complexes.Where, M=Ni (II), Co (II), Cu (II), L= Heterocyclic amine [Quinoline, Pyridine, Iso-quinoline, 2-Picoline and 4- Picoline]. SB=Schiff base ligands such as (SB-A_1)/ (SB-A_2)

Table 1. Physical properties for SB Complexes

Complexes	Colour	Melting point or decomposition temperature (±5°C)	Molar conductance (ohm^{-1} cm^2 mol^{-1})	μ_{eff}(B.M.)
[Ni(SB-A_1)2-pic]	Yellow	250	9.00	2.90
[Ni(SB-A_1)Py]	Red	180	1.28	3.00
[Ni(SB-A_1)Q]	Reddish Brown	210	1.00	3.25
[Co(SB-A_1)IQ]	Greenish Yellow	230	1.50	4.05
[Co(SB-A_2)Q]	Deep Blue	240	2.20	4.00
[Ni(SB-A_2)IQ]	Brown	220	6.50	3.15
[Cu(SB-A_2)Q]	Black	210	5.40	1.90
[Cu(SB-A_2)4-Pic]	Black	240	5.50	1.95

Where, Q = Quinoline , Py = Pyridine, IQ = Iso-quinoline ,2-Pic = 2-Picoline and 4-Pic = 4- Picoline

Table 2. UV-visible spectral bands of the SB complexes

Complexes	Band I (in nm)	Band II (in nm)	Band III (in nm)
[Ni(SB-A_1)2-Pic]	355	412	472
[Ni(SB-A_1)Py]	355	412	472
[Ni(SB-A_1)Q]	355	412	472
[Co(SB-A_1)IQ]	300	400	500
[Co(SB-A_2)Q]	350	420	550
[Ni(SB-A_2)IQ]	340	400	510
[Cu(SB-A_2)Q]	340	420	500
[Cu(SB-A_2)4-Pic]	350	420	520

Where, Q = Quinoline, Py = Pyridine, IQ = Iso-quinoline, 2-Pic = 2-Picoline and 4-Pic = 4- Picoline

Table 3. IR bands for SB Ligands and complexes

Complexes	ν(C=N) cm^{-1}	ν_{asym} (COO) cm^{-1}	ν_{sym} (COO) cm^{-1}	ν_{asym} (N-C) cm^{-1}	ν_{sym}(N-C) cm^{-1}	ν(M-O) cm^{-1}	ν(M-N) cm^{-1}	ν(O-H) cm^{-1}
Ligand(SB- A_1)	1640	1580	1372	-	-	-	-	-
[Ni(SB- A_1)2-pic]	1620	1467	1293	827	745	524	485	3400
[Ni(SB - A_1)Py]	1619	1467	1294	822	745	523	483	3435
[Ni(SB- A_1)Q]	1608	1467	1292	810	744	523	483	3054
[Co(SB - A_1)IQ]	1604	1476	1277	827	746	512	390	3429
Ligand(SB-A_2)	1650	1590	1382					
[Co(SB- A_2)Q]	1620	1509	1377	810	740	529	488	3434
[Ni(SB- A_2)IQ]	1633	1500	1278	826	750	535	484	3324
[Cu(SB- A_2)Q]	1607	1508	1313	810	759	523	399	3446
[Cu(SB- A_2)4Pic]	1619	1506	1231	814	758	578	493	3449

Where, Q = Quinoline, Py = Pyridine, IQ = Iso-quinoline, 2-Pic = 2-Picoline and 4-Pic = 4- Picoline

Table 4. Antibacterial activity of the complexes and *Kanamycin*

Complexes	Zone of inhibition, diameter in nm			
	Gram Negative		Gram Positive	
	E. coli	*Shigella dysenteriae*	*Agro bactrium*	*Bacillus subtilis*
[Ni(SB-A_1)2-Pic]	07	07	10	07
[Ni(SB-A_2)IQ]	07	07	08	08
[Cu(SB-A_2)4-pic]	09	06	08	12
Kanamycin -30	28	20	21	25

Where, IQ = Iso-quinoline, 2-Pic = 2-Picoline and 4-Pic = 4- Picoline

Table 5. Antifungal activity of the complexes against Saccharromycess (SC), Aspergillus niger (AN), Candida albicaus (CA)

Complexes	Diameter of zone inhibition (mm) 200µg/disc		
	SC	AN	CA
[Ni(SB- A_1)2-pic]			
[Ni(SB- A_2)IQ]	12	14	18
[Cu(SB- A_2)4-Pic]	10	9	9
	Very poor	-	-

Where, IQ = Iso-quinoline, 2-Pic = 2-Picoline and 4-Pic = 4- Picoline

Antibacterial, antifungal and cytotoxic activity of the metal complexes

Complexes of several transition metal salts with tridentate ONS donor Schiff base ligands were synthesized and biological activity were studied by Gangadhar B *et al*., (2008) and Prakash Gouda Avaji *et al*., (2009).

The susceptibility of microorganism to antimicrobial agents can be determined *in vitro* by a number of methods. The disc diffusion technique is widely acceptable for preliminary investigations of compounds, which are suspected to possess antimicrobial properties. Antimicrobial activities of the test samples are expressed by measuring the zone of inhibition observed around the area.

Table 6. Brine shrimp lethality bioassay for test complexes

	24 h Exposure
Complexes	LC_{50} (µg/mL)
[Ni(SB- A_1)2-pic]	14.45
[Co(SB- A_1)IQ]	16.98
[Ni(SB- A_2)IQ]	20.41
[Cu(SB- A_2)Q]	14.45
[Cu(SB- A_2)4-Pic]	13.18

Where, Q = Quinoline, IQ = Iso-quinoline ,2-Pic = 2-Picoline and 4-Pic = 4- Picoline

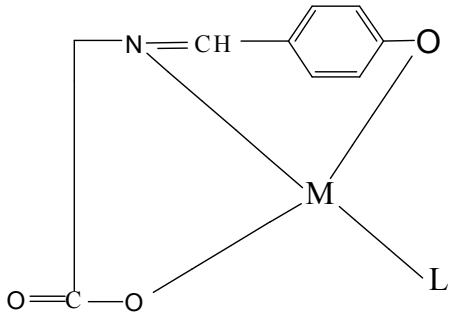


Fig. 1. Square planar structure of the complexes, Where, M=Ni (II), Co (II), Cu (II), L= Heterocyclic amine [Quinoline, Pyridine, Iso-quinoline, 2-Picoline and 4- Picoline]. SB=Schiff base ligands such as (SB-A1)/ (SB-A2)

The present results revealed that the complexes are more microbial toxic than the free metal ions or ligands. The Co (II), Ni (II) and Cu (II) metal Schiff bases complexes Table 4 showed moderate to strong activity against both Gram positive and Gram negative bacteria compared to standard Kanamycin. The results of the antifungal activity of the complexes are recorded in Table 5. From the zone of inhibition it is observed that all the complexes showed significant activity towards all the fungi used. The highest antifungal activity was shown in the complex [Ni (SB- A_1) 2-pic] against Candida albicaus (18 mm).Complex [Co (SB- A_1) IQ] exhibits maximum toxic to brine shrimp compared to other complexes Table 6.

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