

ANTIMICROBIAL STUDIES OF Co (II), Ni (II), Cu (II) AND Zn (II) COMPLEXES DERIVED FROM SCHIFF BASES OF 3-FORMYL QUINOLINE AND 3-HYDRAZINOQUINOXALIN-2(1H) ONE

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ABSTRACT

Cobalt(II), nickel(II), copper(II) and zinc(II) complexes of two new multi-dentate ligands, 3-{(2E)-2-[(2-hydroxyquinolin-3-yl)methylidene]hydrazinyl}quinoxalin-2-ol(QZOH) and 3-{(2E)-2-[(2-sulfanyl quinolin-3-yl)methylidene]hydrazinyl}quinoxalin-2-ol(QZSH) were prepared and characterized by elemental analysis, conductance, thermal, spectral and magnetic data. The ligand QZOH de-protonates to give a monobasic ONO donor and binds to the divalent metal ions in bis-tridentate fashion, using two ONO donor sets. The other ligand QZSH also de-protonates to give a monobasic SNO donor and binds to the divalent metal ions in bis-tridentate fashion, using two SNO donor sets. Octahedral geometries are proposed for all these complexes, and preliminary studies show that they possess potential antimicrobial activity.

Keywords: Quinoline, Quinoxaline, monobasic tri-dentate, antimicrobial.

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INTRODUCTION

Quinoxaline derivatives exhibit a wide variety of biological activities. It has been reported that some quinoxalines demonstrated antibacterial, antifungal, antiviral, antineoplastic, antidepressant, hypoglycemic, anti-inflammatory, excitatory amino acid antagonistic, antiglaucoma, antiparasite, antituberculosis, anticancer, and anti HIV-1 activities¹⁻¹³.

However literature survey revealed that Schiff base containing Quinoxaline and Quinoline has not been prepared and studied so far. Thus the present study deals with synthesis and characterization metal complexes derived from Schiff bases of 2-substituted-3-formyl Quinoline and 3-hydrazinoquinoxalin-2(1H) one.

EXPERIMENTAL

All the reagents are of reagent grade were used as received. All the chemicals and solvents used were dried and purified by standard methods, and moisture was excluded from the glass apparatus using CaCl₂ drying tubes.

Synthesis of 1,4-Dihydroquinoxaline -2,3- dione

A solution of oxalic acid dihydrate (0.238mole, 30g) in H₂O (100ml) was heated to 100°C and conc.HCl(4.5ml) was added, followed by Ophenylendiamine (0.204 mole, 22g) with stirring, temperature was maintained at 100°C for 20 min. the mixture cool by addition of ice. The precipitate was formed and washed with water. Crystallized from 5% NaOH /dil.HCl, yield : 98%, m.p. = >300°C, color: white.

Synthesis of 3-hydrazinoquinoxalin-2(1H) one (a)

A mixture of the 1,4-Dihydroquinoxaline-2,3- dione (0.062mole, 10.04g), hydrazine hydrate 99.9% (1mole, 50ml.) and water (50ml) was heated under reflux for 2h, then cooled to room temperature, the precipitate was filtered, washed with water and crystallized from 2-butanol. m.p: >300°C, yield: 84%, color: yellow needles.

Synthesis of 2-chloro-3-formyl Quinoline(b)

This compound was synthesized by Vilsmier reaction using acetanilide, POCl₃ and DMF at 80^oC as per the procedure given in the literature¹⁴. Yellow crystals (ethyl acetate), yield= 92.24%, m.p. = 172-173^oC.

Table-1: Analytical, magnetic, conductance and electronic data of the Schiff bases and their Cu (II), Ni (II), Cu (II) and Zn (II) complexes.

Code	Ligand/ complex	C% Calc. (Found)	H% Calc. (Found)	N% Calc. (Found)	M% Calc. (Found)	Molar cond. Ohm ⁻¹ cm ⁻² mole ⁻¹	μ _{eff} (BM)	Electronic Spectra (Band maxima) cm ⁻¹
L ₁	QZOH	65.25 (66.97)	3.95 (3.68)	21.14 (21.98)	-	-	-	38760
1	[Co(QZOH) ₂]	60.09 (61.56)	3.36 (3.05)	19.47 (19.78)	8.19 (7.98)	8.31	4.80	8954, 16260, 19,165 ⁴ T _{1g} (F) → ⁴ A _{2g} , ⁴ T _{1g} (F) → ⁴ T _{1g} (P).
2	[Ni(QZOH) ₂]	60.11 (61.87)	3.36 (3.20)	19.47 (19.97)	8.16 (7.49)	6.08	3.20	10256, 16302, 24691 ³ A _{2g} → ³ A _{1g} (F), ³ A _{2g} → ³ T _{1g} (P)
3	[Cu(QZOH) ₂]	59.71 (61.64)	3.34 (3.17)	19.34 (19.82)	8.77 (7.91)	8.12	1.77	17123, 25548, 33670 ² T _g ← ² E _g , Charge transfer
4	[Zn(QZOH) ₂]	59.55 (61.68)	3.33 (3.14)	19.29 (19.86)	9.01 (8.42)	7.17	Dia	-
L ₂	QZSH	62.23 (63.21)	3.77 (3.14)	20.16 (21.34)	-	-	-	37879
5	[Co(QZSH) ₂]	57.52 (59.53)	3.22 (2.87)	18.63 (19.46)	7.84 (7.11)	7.42	5.02	8968, 16250, 19,182 ⁴ T _{1g} (F) → ⁴ A _{2g} , ⁴ T _{1g} (F) → ⁴ T _{1g} (P).
6	[Ni(QZSH) ₂]	57.54 (59.62)	3.22 (3.05)	18.64 (19.37)	7.81 (7.34)	6.33	3.28	10256, 16455, 24691 ³ A _{2g} → ³ A _{1g} (F), ³ A _{2g} → ³ T _{1g} (P)
7	[Cu(QZSH) ₂]	57.17 (59.23)	3.20 (2.88)	18.52 (19.40)	8.40 (7.90)	7.31	1.79	17198, 25974, 30121 ² T _g ← ² E _g , Charge transfer
8	[Zn(QZSH) ₂]	57.03 (59.08)	3.19 (3.01)	18.47 (19.21)	8.63 (7.97)	7.92	Dia	-

Synthesis of 2-hydroxy-3-formyl Quinoline(c)

2-Chloro-3-formyl Quinoline(0.1mol) was refluxed for 10h in HCl(4M) and allowed to cool to room temperature. The reaction mixture was poured into crushed ice to get yellow product¹⁵. Recrystallized from aqueous acetic acid. Yield=89%, m.p.= 295-297^oC.

Synthesis of 2-Mercapto-3-formyl Quinoline(d)

A mixture of 2-Chloro-3-formyl Quinoline (5.73g, 29.98mmol) and sodium sulphide (8.4g, 9.2mmol) was refluxed for 10min on a water bath in ethanol (50ml). Conc. HCl (15ml) was added dropwise to the reaction mixture. The mercapto compound precipitates as a yellow crystalline solid which was further filtered, washed with ethanol, dried and crystallized from ethyl acetate and benzene (8:2)¹⁶. Yield= 84%, m.p. = 193^oC.

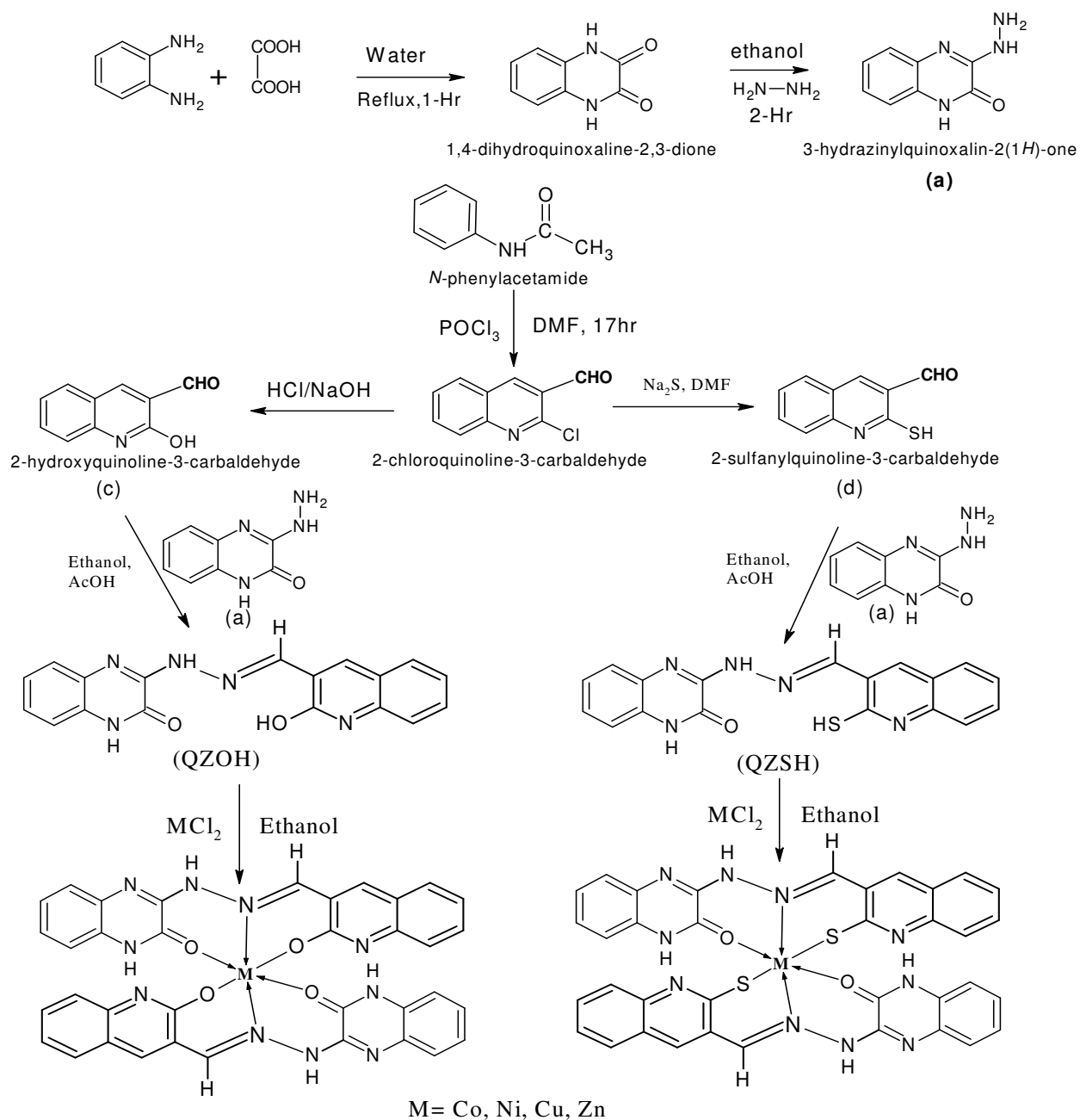
Synthesis of Schiff bases (QZOH and QZSH)

The Schiff base QZOH was synthesized by the condensation of 3-hydrazinoquinoxalin-2(1H) one(a) (0.1M) and 2-hydroxy-3-formyl Quinoline (c)(0.1M) in ethanol under reflux for 6 hours at a pH of 5.5-6.0

using acetic acid. The purity was checked by TLC (Hexane: Ethyl acetate). The Schiff base QZSH was also synthesized by the above said method using 3-hydrazinoquinoxalin-2(1H) one (a) (0.1M) and 2-mercapto-3-formyl Quinoline(d)(0.1M).

Synthesis of transition metal complexes

For the Synthesis of transition metal complexes, hot ethanolic solution of the respective metal(II) chlorides(0.01mol) and the Schiff bases(0.02mol) were refluxed for 4h on a water bath at the pH 7.0-7.7 and the precipitate was filtered, washed successively with ethanol and ether and finally dried over fused CaCl_2 in vacuum. Yield of all the complexes lie in the range of 67-73%.



Scheme-1

RESULTS AND DISCUSSION

All the Co(II), Ni(II), Cu(II) and Zn(II) complexes are coloured, stable, non-hygroscopic and insoluble in common organic solvents like methanol, ethanol, acetone, benzene etc. but soluble in DMF and DMSO. The elemental analysis shows that all the complexes have 1:2 stoichiometry of the type ML_2 . The molar conductance data are too low to account for any dissociation of the complexes in DMF, indicating non electrolytic in nature. The magnetic measurement for Co(II) complexes exhibit magnetic moment values of 4.80-5.02 B.M., Ni(II) complexes showed the magnetic moment values of 3.20-3.28 BM, the Cu(II) complexes showed magnetic moment value of 1.77-1.79 BM, Which shows that the metal complexes shows octahedral geometry. The electronic spectra of all the complexes also support for their octahedral geometry (Table-1).

Biological Studies

In Vitro antibacterial and antifungal assay:

The synthesized Schiff bases and their Co(II), Ni(II), Cu(II) and Zn(II) complexes were studied for their antibacterial and antifungal activities by potato dextrose agar diffusion method. The antibacterial and antifungal activities were done at 100, 50 and 25 mgL^{-1} concentrations in DMF solvent using two bacteria (*Escherichia coli*, *Staphylococcus aureus*) and two fungi (*Aspergillus niger* and *Penicillium chrysogenum*) strains by zone of inhibition method. These bacterial and fungi strains were incubated for 24h and 48h at 37°C respectively. Standard antibacterial (*Gentamycin*) and antifungal drugs (*Fluconazole*) were used for comparison under similar conditions. Activity was determined by measuring the diameter of the zone of inhibition (mm).

The results reveal that the metal complexes show higher activity than their corresponding ligands. The copper complex show highest activity i.e. 73.75 and 71.37% zone of inhibition against the bacterial stains at 100 μ g concentration, which is more than the ligand activity. In antifungal studies, copper complexes exhibits extremely high activity, 100% zone of inhibition against *A. Niger* which is as good as the internal standard at all the concentrations.

CONCLUSIONS

Due to insolubility in water and common organic solvents, all the complexes are thought to be polymeric in nature. The tentative structures of all the complexes are based on elemental analysis, IR, 1H NMR, electronic, magnetic measurements, thermal studies and mass spectra. On the basis of different techniques, it is proposed that all the complexes possess octahedral geometry (Scheme-1) and the Schiff bases act as versatile tridentate ligands coordinated to metal ion through carbonyl oxygen, nitrogen, oxygen and sulphur atoms.

The electrochemical properties of the metal complexes investigated in DMF showed most significant two-electron transfer processes. From the in vitro antibacterial and antifungal activity against representative bacterial and fungal strains, it is evident that the Copper compounds were most active towards the bactericidal activity than other complexes.

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