



Synthesis, Biological Evaluation and Electrochemical Studies of Cu (II) and Ni (II) Complexes of N', N''-1, 2-Diphenylethane-1, 2-diylidenedibenzohydrazide

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ABSTRACT

New tetra-dentate Schiff base N', N''-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (1) was synthesized by the condensation of benzil with isonizide. Further ligand (1) was converted into Cu (II) complex with N', N''-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (2) by treatment of (1) with CuCl₂·2H₂O and in another route Ni (II) complex with N', N''-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (3) was synthesized with reaction of (1) with NiSO₄·7H₂O. Polarographic studies of Cu (II) and Ni (II) complexes with ligand have been done in alcoholic medium and the stability constant log β values were found for Cu (II) and Ni (II) complexes. Ligand and complexes were characterized by IR and ¹HNMR, and complexes tested for biological activity.

Keywords: Benzil, Schiff base, Polarograph and Stability constant.

INTRODUCTION

A great deal of work has been reported on the synthesis and characterization of different types of Schiff base complexes with transition and non transition elements. [1-3] The majority of Schiff bases usually act as multidentate N-N and N-O donors with the formation of mono-or polynuclear complexes. [4-6] In addition to their interesting ligational properties, both Schiff bases and their complexes have important biological and industrial applications. [7-9]

MATERIALS AND METHOD

Apparatus

Melting points were taken in open capillary tubes and are therefore uncorrected. Purity of the compounds was checked on silica gel TLC plates of 2 mm thickness using n-hexane and ethyl acetate as solvent system. The visualization of spot was carried out in an iodine chamber. The IR spectra were recorded on Perkin- Elmer spectrometer. The ¹H NMR spectra were scanned on a Bruker DRX-300 MHz spectrometer (300 MHz) in (CDCl₃) using TMS as internal standard and chemical shifts are expressed in δ ppm.

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The title compounds (1-3) were screened for their antibacterial and antifungal activities using cup and well method. [9] Antibacterial activity of compounds (500µg/ml) has been evaluated against four bacterial strain viz. *E. coli*, *P. aeruginosa*, *S. typhi* and *B. subtilis*. Almost all the compounds showed low to moderate activity against *E. coli*, *P. aeruginosa* and *S. typhi*. Screening of the title compounds (500µg/ml) for antifungal activity was carried out against two fungal strain viz. *A. fumigates* and *C. albicans* using flucanazole as a standard drug. Compounds 1-3 were good to moderate active against *A. fumigatus*. and *C. albicans* (Table 3).

Synthesis of N', N''-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide

Schiff bases have been synthesized by condensing the ethanolic solution of benzil (0.01mol) and isonizide (0.02 mol) and add catalytic amount of acetic acid (1 ml). The condensation product was filtered, washed with ethanol and ether, recrystallized with ethanol, and dried under reduced pressure. Purity of the compounds was monitored by TLC using silica gel G. Schiff bases have been characterized by elemental and IR and ¹HNMR spectra.

Yield 72%, Colour- white, m.p.172

IR (KBr): 3242 (NH), 3056 (Ar-CH=CH), 1679 (CONH), 1601 (C=N),

¹HNMR δ: (6.72-7.24 m, 10H, Ar-CH=CH), (4.53 s, 1H, CONH)

Synthesis of Cu (II) complex with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (2)

The Cu (II) complex has been prepared by mixing the methanolic solution of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.015 mol) and to the methanolic solution of Schiff bases (0.01 mol). The resulting mixture was then refluxed on water bath for 10-12 hours. The precipitated complexes were recrystallized with ethanol, finally washed with petroleum ether (60-80°C), and dried under reduced pressure.

Yield 59%, Colour- brown, m.p. 123°C.

IR (KBr): 3250 (NH), 3067 (Ar-CH=CH), 1675 (CONH), 1612 (C=N),

$^1\text{H NMR}$ δ : (6.82-7.29 m, 10H, Ar-CH=CH), (4.55 s, 1H, CONH)

Synthesis of Ni (II) complex with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (3)

The Ni (II) complex has been prepared by mixing the methanolic solution of $\text{NiSO}_4 \cdot 7\text{H}_2\text{O}$ (0.015 mol) and to the methanolic solution of Schiff bases (0.01 mol). The resulting mixture was then refluxed on water bath for 10-12 hours. The precipitated complexes were recrystallized with ethanol, finally washed with petroleum ether (60-80°C), and dried under reduced pressure.

Yield 52%, Colour- yellow, m.p. 138°C.

IR (KBr): 3249 (NH), 3062 (Ar-CH=CH), 1671 (CONH), 1606 (C=N),

$^1\text{H NMR}$ δ : (6.79-7.31 m, 10H, Ar-CH=CH), (4.59 s, 1H, CONH)

Polarographic studies of Cu (II) and Ni (II) N', N"-1, 2-diphenylethane-1, 2-diylidene dibenzohydrazide complex

A systronics polarograph 1632 was used for obtaining C.V. curves. metal solution (1mM) were prepared using $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and $\text{NiSO}_4 \cdot 7\text{H}_2\text{O}$ and ligand solution was prepared by dissolving N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (0.01 mol) in methanol. Citric acid and Na_2HPO_4 solution were used as buffer to maintain pH. Ionic strength was kept constant by using KCl as supporting electrolyte. Gelatin (0.002%) was used as maximum suppressor. The capillary had following characteristics $T=1$ drop/sec. IR drop correction were applied. Solution was deaerated by purging of oxygen free nitrogen through the polarographic cell.

Determination of half wave potential of Cu (II) with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide

1×10^{-3} M Cu (II) solution in N/10 KCl has been used to obtain polarogram of Cu (II). This showed $E_{1/2}$ at - 0.25 Vs. SCE. Polarographic studies were done on Cu (II) with various concentration of N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide. The polarographic waves showed the half wave potentials shifted towards more negative value with increasing concentration of ligand indicated complex formation and the diffusion current was found to decrease regularly with increase of N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide concentration.

Determination of half wave potential of Ni (II) with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide

1×10^{-3} M Co (II) solution in N/10 KCl has been used to obtain polarogram of Ni (II). This showed $E_{1/2}$ at - 1.3 Vs. SCE. Polarographic studies were done on Ni (II) with various concentration of N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide. The polarographic waves showed the half wave potentials shifted towards more

negative value with increasing concentration of ligand indicated complex formation and the diffusion current was found to decrease regularly with increase of N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide concentration.

Table 1: Polarographic characteristics of Cu (II) complex with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide

S. No	Cx	Log Cx	$E_{1/2}$	Log β
1	0.00	0.00	0.250	-
2	0.01	-2	0.30	12.16
3	0.015	-1.8239	0.32	11.15
4	0.020	-1.6987	0.335	10.47
5	0.025	-1.6020	0.355	10.32
6	0.030	-1.5228	0.370	9.54
7	0.035	-1.4559	0.390	9.20
8	0.04	-1.3979	0.405	8.91
9	0.045	-1.3467	0.420	8.65

Table 2: Polarographic characteristics of Ni (II) complex with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide

S. No	Cx	Log Cx	$E_{1/2}$	Log β
1	0.00	0.00	1.150	-
2	0.01	-2.0	1.250	11.38
3	0.015	-1.8239	1.255	10.85
4	0.020	-1.6987	1.260	10.52
5	0.025	-1.6020	1.265	10.30
6	0.030	-1.5228	1.278	10.42
7	0.035	-1.4559	1.285	10.40
8	0.04	-1.3979	1.3254	11.52
9	0.045	-1.3467	1.335	11.65

Table 3: Antimicrobial activity of synthesized compounds 1-3
Antimicrobial activity, Zone of inhibition (mm)

Compd	<i>B. subtilis</i>	<i>E. coli</i>	<i>S. typhi</i>	<i>P. aeruginosa</i>	<i>A. fumigatus</i>	<i>C. albicans</i>
1	+++	++	+	++	++	++
2	++	+	--	+	+++	++
3	++	+	--	--	+	+++
STD ₁	+++	+++	++	+++	--	--
STD ₂	--	--	--	--	++	+++

Zone of inhibition (mm): + = 10-14 (poor activity), ++ = 15-18 (moderate activity), +++ = 19-22 (good activity), ++++ = 23-26 (strong activity).
Standard: STD₁ = Ciprofloxacin, STD₂ = Flucanazole

RESULTS AND DISCUSSION

Benzil reacted with isonizide in absolute alcohol to give N, N-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (1). This show intense bands at 3242 (NH), 3056 (Ar-CH=CH), 1679 (CONH), group respectively in IR region. Ligand (1) reacted with $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ and $\text{NiSO}_4 \cdot 7\text{H}_2\text{O}$ and gave complexes Cu (II) with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide (2) and Ni (II) with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzo hydrazide (3). These complexes showed medium to good activity against antibacterial and fungal activity.

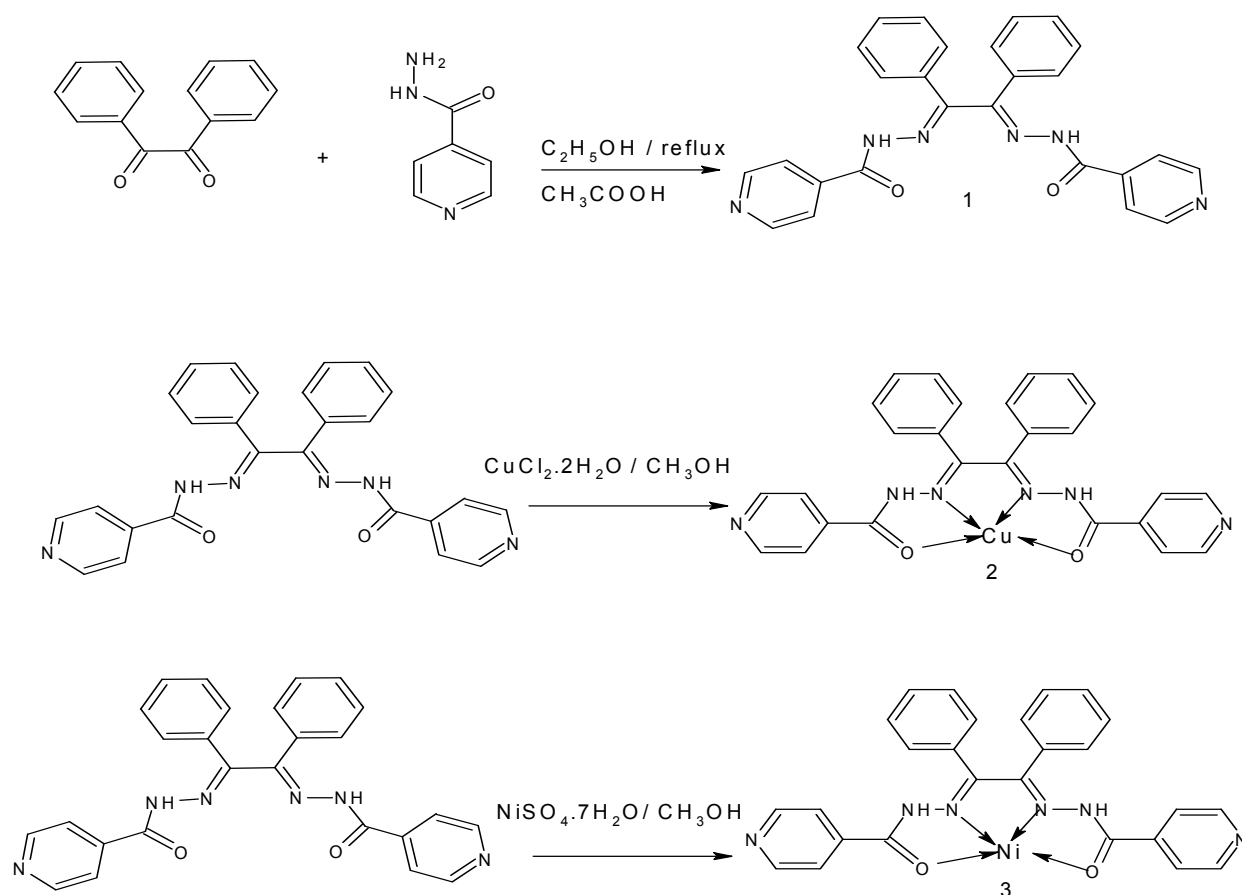
(a) Verification of diffusion controlled nature (by Illkovic equation) id Vs C and id Vs $\sqrt{t}$ plots.

(b) The Heyrovsky –Illkovic equation showed the reversible nature of reduction process involving two electrons means the value of n is 2 for both the systems.

$$E = (E_{1/2}) - 0.591/n \log i/d$$

(c) A single wave is obtained for Cu (II) and Ni (II) complexes with N', N"-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide system between pH 6.5 to 7.1 and 7.5 to 8.5 respectively.

(d) Determination of coordination number: The plots of $E_{1/2}$ Vs log Cx have been found to be a straight line showing the



Reaction Scheme 1

formation of most stable complexes in both the system. The value of j as determined by slope is 4 for both systems. This shows that the composition of complexes is in 1:1 (M: L) ratio and tentative structure of the complexes are given in Reaction Scheme 1

(e) Determination of stability constant for both Cu (II) and Ni (II) complexes with N, N'-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide system:

The stability constants of the Cu (II) and Ni (II) complexes with N, N'-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide complexes have been determined by classical method of Lingane⁸. The $E_{1/2}$ has a linear correlation with ligand concentration which shows that there is only complex formed. The following equation has been used to calculate the stability constant of the complexes studied.

$$\Delta(E_{1/2}) = .591/n \log \beta + j .591/n \log C_x$$

Thus the values of $\log \beta$ have been found to be 10.05 and 10.88 for Cu (II) and Ni (II) complexes respectively with N,N'-1,2-diphenylethane-1,2-diylidenedibenzohydrazide. Polarographic characteristics of Cu (II) and Ni (II) complexes with N, N'-1, 2-diphenylethane-1, 2-diylidenedibenzohydrazide complexes are given in Table I and II.

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