



**MICROWAVE ASSISTED SYNTHESIS, CHARACTERISATION AND BIOLOGICAL ACTIVITIES ON COMPLEXES OF CU (II) WITH LIGANDS DERIVED FROM 2-(ETHYLAMINO) PYRIDINE**

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**Abstract:**

The importance and versatility of ligands with amide groups contributed to the selection of this category of ligands and their complexes for the purpose of research. The synthesis, spectroscopic analysis, and biological investigations of amide complexes containing Cu (II) ions that are generated from heterocyclic amines are presented in this article. It has been possible to synthesis four ligands derived from 2-(Ethylamino) pyridine including their complexes with Cu (II). According to the green chemistry approach, a microwave irradiation technique for the production of complexes has been devised. The complexes have been described by elemental analysis, infrared, electronic, ESR spectra, and magnetic susceptibility investigations. The  $n \rightarrow \pi^*$  transition of the chromophoric C=O group of the amide bond is responsible for the distinctive band seen in the UV spectra of the uncomplexed amide group containing ligands in the 208-220 nm area. The copper complexes containing ligands throughout the entire amide group exhibit a bathochromic shift in this band. IR investigations suggest that the carbonyl group plays a role in metal complexation, which is why this shift occurred. All complexes exhibit a strong band at approximately  $25000 \text{ cm}^{-1}$ , which can be attributed to the  $M \leftarrow L$  charge transfer transition originating from the ligand's 'O' atom to Cu (II). However, uncomplexed ligands also exhibit a band in the same region, suggesting that either the charge transfer band is absent in the complexes or it has been overlapping by the intraligand transition band. The electronic spectra data were very helpful in indicating that the complexes octahedral geometry was deformed. This supposition was also confirmed by the magnetic moment measurements & EPR spectra. The antibacterial activity of the ligands that were produced and their novel metal complexes against *Staphylococcus aureus* and *Escherichia coli* has been evaluated in vitro. The outcome demonstrates that, when applied to these bacteria, all Cu (II) complexes are effective antibacterial agents.

**Keywords:**

Copper (II), Microwave irradiation, Amide, antibacterial

**INTRODUCTION**

An amide group or bond connects an amino acid residue to its neighbor in a protein. With our growing understanding of protein structure, the amide group's remarkable capacity to bind metal ions has come to light. This is mostly because of the following details:

- (i) The amino group is an essential component of many biomolecules. Additionally, amido group-containing ligands have been identified as potential chelating agents. These ligands are potential analogs of important complexes found in nature, such as metal carrier proteins and antimicrobial peptides. (1-2)
- (ii) Through complexation, they modify the metal cluster redox potential to higher positive values, ensuring the stability of the metal ions in their highly oxidized forms. According to earlier research, the procurement of trivalent copper becomes easier when it is coupled by deprotonated amido groups rather than by an amine nitrogen atom. This is mostly due to a ligand field effect and does not simply happen because the complex is reduced. In conclusion, it can be that compounds like amide or peptides, which contain negatively charged nitrogen atom and can encourage deprotonation, should be regarded as ligands coordinated chemists who may find them useful in stabilizing metal cations in extremely high oxidation states.



(iii) They provided dioxamide fragments with link [-HN-CO-CO-NH-], which eventually polymetallic system among fascinating magnetic property. (3-7)

Copper is a common metal that occurs naturally in the environment and spreads through natural processes. Copper is a very important micronutrient that acting a role in a range of biological process, include embryonic development, mitochondrial respiration, hemoglobin regulating, and hepatocyte and brain activities. Copper that has been oxidized (II) and copper that has been reduced (I). Copper has a special property that makes it suitable for a wide range of biological systems. In the sphere of biological activity, copper plays an essential function. This paper describes the synthesis, spectroscopic analysis, and antibacterial studies of Cu (II) complexes with amide-group-containing ligands. The complexes have been characterized on the basis of elemental analysis, infrared spectra, electronic spectra, and magnetic susceptibility measurements.

## EXPERIMENTAL

All the chemicals and solvents used were of AR grade. TLC has been used to confirm the synthesized compounds purity. The IR spectra was captured on Bruker optical model alpha (FT-IR) (Zn-Se optics, ATR) (4000-500 cm<sup>-1</sup>) Spectrophotometer in KBr disc. The ligands <sup>1</sup>H-NMR spectra at room temperature were captured on Bruker DRX-300 (300 MHz) FT-NMR with low and high temperature Facility (-90°C to 80°C). Parts per million (ppm) are the units used to report the chemical shifts. Vibrating sample magnetometer (VSM) model 155 magnetic susceptibility investigations were performed at 5500 Gauss field strength. Microwave synthesis was carried out in domestic microwave oven. Beck Man DU-64 Spectrophotometer, with quartz cell of 10mm light path was used for absorption measurement.

**Synthesis of ligands by microwave irradiation:** Four ligands i.e. 2-chloro-N-ethyl-N-(pyridine-2-yl)benzamide (NENP2CB), 2-bromo-N-ethyl-N-(pyridine-2-yl)benzamide (NENP2BB), 4-chloro-N-ethyl-N-(pyridine-2-yl)benzamide (NENP4CB), 4-bromo-N-ethyl-N-(pyridine-2-yl)benzamide (NENP4BB) were synthesized. To produce the amide ligand, the acid chloride solution has been mixed with the amine solution (0.055 mol in 15 ml ethanol). The reaction mixture was refluxed over a heating element (60-65°C) for around six hours. After cooling, the crystals were separated, re-crystallized with alcohol, and dried under vacuum. The purity of the chemical was assessed by utilizing the TLC method in several solvents.

## MICROWAVE IRRADIATION SYNTHESIS OF Ni (II) COMPLEXES

In order to synthesize Cu (II) complexes with various ligands (i.e. NENP2CB, NENP2BB, NENP4CB, and NENP4BB), a 250 mL round-bottom flask containing 0.001 mole of nickel perchlorate and 30 mL of ethanol was filled with the corresponding ligand (0.002 mol) and stirred continuously. The resulting mixture was irradiating the reaction mixture on an alumina bed for 2 to 10 minutes at 600 W in a home microwave oven, or exposing the reaction mixture's slurry in a microwave reactor at 600 W while maintaining various intervals of time for the occasional end or definitive inspection of TLC data. Methanol was used to purify, recrystallize, and dry the crystals under vacuum. Additionally, complexes and ligands were produced using the conventional method, with good results.

## RESULTS AND DISCUSSION

It was determined that every complex that was created was a colored crystalline or powder that was insoluble in most organic solvents and water, except for DMF and methyl alcohol. It was also shown to be stable for an extended amount of time under standard laboratory settings. Table 1 displays the physical characteristics and elemental analysis findings. The analytical findings and the complexes suggested molecular formula correlate rather well. Generally speaking, the microwave process produced superior results and required far less time than the traditional procedure.

**Table 1: Physical and analytical data of Cu (II) complexes**

S.	Complexes	Colour	M.P. (°C)	Reaction period	Yield (%)	R <sub>f</sub> value	Elemental analysis % cal. (found)
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No.				C.M. (h)	M.M. (min.)	C.M.	M.M.		Cu	C	H	N
1.	[Cu-(NENP2CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	Red	360	7	2.30	50.12	63	(0.889) <sup>g</sup>	10.23 (10.02)	54.15 (52.14)	4.87 (4.56)	9.02 (8.46)
2.	[Cu-(NENP2BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	Green	92	6.5	2.45	93.63	89	(0.669) <sup>b</sup>	8.95 (7.89)	47.37 (47.01)	4.26 (4.13)	7.89 (7.09)
3.	[Cu-(NENP4CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	Brown	112	7.5	3.10	5014	61	(0.789) <sup>h</sup>	10.23 (9.97)	54.15 (53.58)	4.87 (3.98)	9.02 (8.73)
4.	[Cu-(NENP4BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	Dark Green	98	6.5	2.10	71.36	85	(0.864) <sup>h</sup>	8.95 (8.12)	47.37 (47.17)	4.26 (3.72)	7.89 (6.67)

**b = Ethyl acetate: Carbon tetrachloride (4: 6), g = Acetone: Carbon tetrachloride (6: 4), h = acetone: carbon tetrachloride (7:3)**

**C.M. = Conventional Method, M.M. = Microwave Method**

**Vibrational spectra:** Tables: 3 provide specific infrared spectral bands, The amide  $\nu$  (N-H) mode's infrared bands, which are seen around 3345-3421 cm<sup>-1</sup> for free amide ligands, are pushed towards higher frequencies, suggesting that the nitrogen atoms are not involved in coordination. The participation of carbonyl oxygen of the amide-I group in metal ligand bonding is demonstrated by the 25-45 cm<sup>-1</sup> negative shift in the amide-I ( $\nu$  C=O) frequency in complexes relative to ligands. Even though the two modes are linked, the amide II and III bands from the  $\nu$  (C-N) and  $\delta$  (N-H) modes shift towards higher frequencies, further confirming the coordination of the amide group via carbonyl oxygen. The decrease in the double bond characteristic of C=O and the consequent increase in the double bond character of C-N may account for these facts. The complexes infrared spectra reveal a band that corresponds to  $\nu$  (C-O), which is not present in the ligand's spectra.

Pyridyl nitrogen contributes in bonding in complexes, as evidenced by the complexes 15-40 cm<sup>-1</sup> negative shifting of the pyridine ring peak relative to ligands.

**Table 2: IR Spectral data of ligands and its Cu (II) complexes**

S. No.	Ligands Complexes	$\nu$ C-O <sup>p</sup>	$\nu$ C-N + $\delta$ N-H <sup>q</sup>	$\nu$ N-H + $\delta$ C-N <sup>r</sup>	$\nu$ N-H (amide)	pyridyl ring	$\nu$ Cu-O	$\nu$ Cu-N	Miscellaneous band
1.	NENP2CB	1707	1395	-	3429	1460	-	-	-
	[Cu-(NENP2CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1639	1456	1331	3428	1420	687	458	867 and 627 coordinated water
2.	NENP2BB	1691	1380	1306	3321	1540	-	-	-
	[Cu-(NENP2BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1622	1495	1376	3318	1532	682	491	866 and 627 coordinated water
3.	NENP4CB	1679	1377	1292	3228	-	-	-	-
	[Cu-(NENP4CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1627	1511	1379	-	-	659	501	866 and 628 coordinated

									Water
	NENP4BB	1710	1491	1279	3421	1560	-	-	-
4.	[Cu-(NENP4BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1612	1502	1355	3518	1546	672	536	3421, 825 and 623 coordinated water

**Magnetic moments and electronic spectra:** Bivalent copper compounds magnetic susceptibility has been investigated at ambient temperature. Table 3 displays the magnetic moments for each complex that were determined using the room temperature magnetic susceptibility data. It has been determined that the solid state magnetic moments for each of the amide ligand copper complexes at room temperature fall between 1.76 and 2.02 BM. These data demonstrate that the nature of all copper complexes is paramagnetic. However, only geometrical adoptions of the central metal ion within complexes can result from the values of magnetic moment in conjunction with electronic spectra. The  $n \rightarrow \pi^*$  transition of the chromophoric C=O group of the amide bond is responsible for the distinctive band seen in the UV spectra of the uncomplexed amide group containing ligands in the 208-220 nm area. The copper complexes containing ligands throughout the entire amide group exhibit a bathochromic shift in this band. IR investigations suggest that the carbonyl group plays a role in metal complexation, which is why this shift occurred.

All complexes exhibit a strong band at approximately 25000 cm<sup>-1</sup>, which can be attributed to the M ← L charge transfer transition originating from the ligand's 'O' atom to Cu (II). However, uncomplexed ligands also exhibit a band in the same region, suggesting that either the charge transfer band is absent in the complexes or it has been overlapping by the intraligand transition band. The electronic spectra data were very helpful in indicating that the complexes octahedral geometry was deformed. This supposition was also confirmed by the magnetic moment measurements. Data from EPR spectra provided additional confirmation of this.

Table 3: Magnetic moment and electronic spectral data of Cu (II) complexes

S. No.	Complexes	$\mu_{\text{eff}}$ (BM)	Electronic spectral bands $\lambda_{\text{max}}$ (cm <sup>-1</sup> )	Tentative assignments	Expected geometry
1.	[Cu-(NENP2CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1.84	10536, 10699, 13012, 14164, 17069, 18073, 18358, 18841	<sup>2</sup> E <sub>g</sub> □ <sup>2</sup> T <sub>2g</sub> <sup>2</sup> B <sub>1g</sub> □ <sup>2</sup> A <sub>1g</sub>	Distorted Octahedral
2.	[Cu-(NENP2BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1.95	18255, 18789, 19051	<sup>2</sup> E <sub>g</sub> □ <sup>2</sup> T <sub>2g</sub> <sup>2</sup> B <sub>1g</sub> □ <sup>2</sup> A <sub>1g</sub>	Distorted Octahedral
3.	[Cu-(NENP4CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	1.91	13666, 13783, 14016, 14154, 14269, 14582, 19101	<sup>2</sup> E <sub>g</sub> □ <sup>2</sup> T <sub>2g</sub> <sup>2</sup> B <sub>1g</sub> □ <sup>2</sup> A <sub>1g</sub>	Distorted Octahedral
4.	[Cu-(NENP4BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ](ClO <sub>4</sub> ) <sub>2</sub>	2.02	13281, 13822, 14824, 17512, 20586, 19380, 19012	<sup>2</sup> T <sub>2g</sub> □ <sup>2</sup> E <sub>g</sub> <sup>2</sup> B <sub>1g</sub> □ <sup>2</sup> A <sub>1g</sub>	Distorted Octahedral

**Antibacterial activity:** The antibacterial activity of the compound against *S. aureus* & *E. coli* was tested using Muller Hinton Agar medium. The activity was carried out using paper disc technique represent in Table 4, which shows all the Cu (II) complexes have moderate antibacterial activities against *E. coli* and *S. aureus*.

**Table 4: Biological activity of amide group containing ligands and complexes against E. coli & S. aureus**

S. No	Ligand/Complexes	Against E. coli		Against S. aureus	
		Zone of inhibition (in mm) at different concentration		Zone of inhibition (in mm) at different concentration	
		100 ppm	200 ppm	100 ppm	200 ppm
1.	NENP2CB	0.0	0.0	7.0	6.0
	[Cu-(NENP2CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] (ClO <sub>4</sub> ) <sub>2</sub>	0.0	0.7	3.0	6.0
2.	NENP2BB	9.0	13.0	10.0	7.0
	[Cu-(NENP2BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] (ClO <sub>4</sub> ) <sub>2</sub>	0.0	0.5	5.0	3.0
3.	NENP4CB	4.0	0.0	13.0	5.0
	[Cu-(NENP4CB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] (ClO <sub>4</sub> ) <sub>2</sub>	0.0	0.4	0.4	0.5
4.	NENP4BB	1.0	2.0	4.0	5.0
	[Cu-(NENP4BB) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] (ClO <sub>4</sub> ) <sub>2</sub>	0.0	0.2	6.0	7.0

### CONCLUSIONS

The method of coordination between the amide group's carbonyl oxygen and the pyridyl nitrogen around the metal center in the complexes of all the ligands is revealed by changes in the distinctive infrared bands of amide group containing ligands upon complexation. The infrared spectra indicate that the complexes may involve an exogenous ligand and that coordination may occur due to either deprotonated or non-deprotonated nitrogen. Recapitulating the experimental findings, it is determined that these ligands containing amide groups function as bidentate ligands in the complexes that adopt deformed octahedral geometry, with a stoichiometry of two amide ligand molecules and two exogenous ligand per copper ion. The biological activity of Cu (II) complexes containing ligands with amide groups has been investigated. The traditional disc diffusion technique has been applied to the inquiry. E. Coli and S. Aureus bacterial subcultures have been used to investigate the compounds' antibacterial properties. The study demonstrates that most ligands have more antibacterial activity than complexes, with a few notable exceptions.

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