



## SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF COPPER (II), COBALT (II) AND NICKEL (II) COMPLEXES WITH 2 - AMINOBENZIMIDAZOLE

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**Abstract:** The preparation and properties of some copper(II), cobalt(II) and nickel(II) complexes with 2-aminobenzimidazole (L) are reported. The synthesized complexes are of the general formula:  $[ML_2Cl_2] \cdot nH_2O$ ;  $M=Cu, Co$  or  $Ni$ ;  $n=0$  or  $2$ ). The complexes were characterized by elemental analysis (metal), molar conductivity, magnetic susceptibility measurements and IR spectra. The antimicrobial activity of the benzimidazoles and their complexes were evaluated against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus sp.* and *Saccharomyces cerevisiae*. It is found that some complexes have shown higher antimicrobial activity than ligand.

### Keywords:

benzimidazole, complexes, copper(II), cobalt(II), nickel(II), antimicrobial.

## 1. INTRODUCTION

A wide variety of benzimidazole derivatives have been described for their chemotherapeutic importance. These compounds have shown biological activity against parasites and bacteria. Also, some of them are known to possess antibacterial, antiviral, antiinflammatory, antihypertensive, arteriosclerosis and fungicidal properties. Various benzimidazoles are effective inhibitors of the growth of lactobacilli, vaccinia virus, influenza virus and HIV-virus [2-6,8-12].

In our previous studies [8-11], we also observed that benzimidazole derivatives, as well as their complexes with transition metal ions, have shown considerable biological activity. Following our synthesis and antibacterial works on benzimidazole derivatives and their complexes,

we now report the synthesis, physico-chemical characteristics and antimicrobial activities of copper(II), cobalt(II) and nickel(II) complexes with 2-aminobenzimidazole.

## 2. EXPERIMENTAL

All chemicals used to prepare the complexes were of analytical reagent grade, commercially available from different sources.

### Synthesis of complexes

All the complexes were prepared following the same procedure. A solution of 5mmol  $MCl_2 \cdot 6H_2O$  ( $M=Cu, Co$  or  $Ni$ ) in  $20cm^3$  of EtOH was added into a solution of 10 mmol of the 2-aminobenzimidazole (L) in  $20cm^3$  EtOH. The resulting mixture was boiled under reflux on a water bath for about 2h and then cooled. The complexes were separated from the reaction mixture by filtration, washed with EtOH and dried *in vacuo* over  $CaCl_2$ . The yield of the complexes varied in the range 50-55%.

### Measurement methods

Elemental analysis was carried out by standard micromethods. Magnetic susceptibility measurements were made at room temperature using an MSB-MKI magnetic susceptibility balance (Sherwood Scientific Ltd., Cambridge, England). Molar conductivities of freshly prepared  $1 \cdot 10^{-3} mol dm^{-3}$  solutions (DMF) were measured on a Jenway 4010 conductivity meter. Infrared spectra (KBr pellets) were recorded on an Infrared 457 Perkin-Elmer spectrophotometer.

### Antimicrobial investigations

For these investigations the filter paper disc method was applied. Each of the investigated isolates of bacteria were seeded in the tubes with nutrient broth (NB). The seeded NB ( $1cm^3$ ) were homogenized in the tubes with  $9cm^3$  of melted ( $45^\circ C$ ) nutrient agar (NA). The homogenous suspension was poured into Petri dishes.

The discs of filter paper (diameter 5mm) were ranged on cool. After cooling on the formed solid medium,  $2 \cdot 10^{-5} dm^3$  of the investigated compounds were placed with micropipette. After incubation for 24 hours in thermostat at  $25-27^\circ C$ , inhibition (sterile) zone diameters (including disc) were measured and expressed in mm. Inhibition zone diameter over 8mm indicates the tested compound is active against bacteria under investigation. Every test was done in three replications.

The antimicrobial activities of the investigated compounds were tested against four strains of bacteria (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus sp.* and *Saccharomyces cerevisiae*). In parallel with antimicrobial investigations of the complexes, ligand was

tested too, as well as the pure solvent. The concentration of each solution was  $5 \cdot 10^{-2} \text{ mol dm}^{-3}$ . Commercial DMF was employed to dissolve the tested samples.

### 3. RESULTS AND DISCUSSION

The elemental analysis of complexes, magnetic moments and molar conductance data are summarized in Table 1.

**Table 1.** Some physical characteristics and analytical data of the complexes

Complex	Mr	Colour	M.p. (°C)	$\mu_{\text{eff}}$ ( $\mu_{\text{B}}$ )	$\lambda_{\text{M}}$ *	Metal Found (Calcd.) %
[CuCl <sub>2</sub> L <sub>2</sub> ].2H <sub>2</sub> O	436.45	green	201	1.83	35.6	14.01 (14.56)
[CoCl <sub>2</sub> L <sub>2</sub> ]	395.83	blue	192	4.57	39.9	14.52 (14.88)
[NiCl <sub>2</sub> L <sub>2</sub> ]	395.60	green	196	3.40	79.1	14.27 (14.84)

\* In DMF,  $1 \text{ mmol dm}^{-3}$  solution at  $25^{\circ} \text{C}$ ; in  $\text{Scm}^2 \text{mol}^{-1}$

All the complexes are sparingly soluble in common organic solvents such as alcohols or acetone, but highly soluble in dimethylformamide and dimethylsulphoxide. The complexes were synthesized in the reaction of warm ethanolic solution of the  $\text{MCl}_2 \cdot 6\text{H}_2\text{O}$  ( $\text{M}=\text{Cu}, \text{Co}$  or  $\text{Ni}$ ) with L (2-aminobenzimidazole) in a mole ratio 1:2. It should be noticed that the reaction of the all metal ions yielded bis(ligand) complexes.

The molar conductance values of copper(II) and cobalt(II) complexes in DMF solutions, compared with the values of non-electrolytes, are higher, but considerable less than the molar conductances of 1:1 type of electrolytes. It indicates that one coordinated chloride anion has been replaced by DMF molecule. The molar conductances of nickel(II) complexes fall in the range of  $65\text{-}90 \text{ Scm}^2 \text{mol}^{-1}$ . These values correspond to a 1:1 type of electrolytes in DMF, which also indicates a partial substitution of the coordinated chloride with solvent molecules [11].

#### *Magnetic properties*

An indication of the most probable geometric configuration of the synthesized Co(II) complexes may be their colour and magnetic moments (Table 1). Namely, the blue cobalt(II) complexes usually have a tetrahedral configuration. The magnetic moment values (Table 1) of the cobalt(II) complexes are in the expected range ( $4.2\text{-}4.7 \mu_{\text{B}}$ ) for tetrahedral stereochemistry [11]. The room temperature effective magnetic moments of the nickel(II) complexes are in the range which also

support their tetrahedral geometry. The room temperature effective magnetic moments of the copper(II) complexes are in the range of  $1.73\text{-}2.20\mu_B$ , which corresponds to one unpaired electron typical for tetrahedral geometry.

### *Infrared spectra*

The infrared spectra of the ligand exhibit a band at  $3300\text{-}3100\text{cm}^{-1}$ , assigned to  $\nu(\text{NH})$ . The lowering of this band frequency is due to association through the intermolecular hydrogen bonding [7]. The band appearing at about  $1550\text{ cm}^{-1}$  may be assigned to  $\nu(\text{C}=\text{N})$  vibrations [7]. The infrared spectra of the complexes investigated are similar to those of the corresponding ligand. An upward shift ( $10\text{-}15\text{ cm}^{-1}$ ) of  $\nu(\text{C}=\text{N})$  in the IR spectra of the complexes as compared to their values in the free ligand, suggests coordination through pyridine nitrogen of 2-aminobenzimidazole [1]. The other bands in the spectrum of each complex are similar to those in the corresponding ligand spectrum except for slight shifts in their positions and changes in their intensities due to coordination.

The presented results (molar conductivity, magnetic moments and IR spectra) suggest that all Cu(II), Co(II) and Ni(II) complexes are tetrahedral which is realized by participation of the pyridine nitrogen of two organic ligand molecules and two chloride anions, typical for these classes of organic ligands [8-11].

### *Antimicrobial investigations*

All the complexes were screened for their antimicrobial activities against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus sp.* and *Saccharomyces cerevisiae*. The relevant data are presented in Table 2.

**Table 2.** Antimicrobial activity of the benzimidazole derivatives and their complexes

Compound	<i>Pseudomon. aeruginosa</i>	<i>Staphylococc. aureus</i>	<i>Bacillus sp.</i>	<i>Sacchar. cerevisiae</i>
L	++	∅	∅	∅
$[\text{CuCl}_2\text{L}_2]\cdot 2\text{H}_2\text{O}$	+++	+	+++	∅
$[\text{CoCl}_2\text{L}_2]$	∅	+++	+++	+++
$[\text{NiCl}_2\text{L}_2]$	∅	+	∅	∅

- ∅ - no activity  
 + - low inhibitory activity  
 ++ - middle inhibitory activity  
 +++ - high inhibitory activity

From the data, it is evident that the most active compounds are copper(II) and cobalt(II) complexes. In the case of the *Sacharomyces*

*cerevisiae* only the cobalt(II) complex is antimicrobial active. On comparing the biological activity of the ligand and its complexes, it was found that some complexes are more effective against the bacteria. From the results, it can be concluded that nickel(II) does not increase the general antibacterial activity of the organic ligand.

The higher activity of the some complexes, as compared to the free ligand, can be understood in terms of the chelation theory. This theory explains that a decrease in the polarizability of the metal could enhance the lipophilicity of the complexes.

#### 4. CONCLUSION

2-aminobenzimidazole with copper(II), cobalt(II) and nickel(II) formed complexes of the general formula  $[ML_2Cl_2] \cdot nH_2O$ ;  $M=Cu, Co$  or  $Ni$ ;  $L=2$ -aminobenzimidazole;  $n=0$  or  $2$ ). All the complexes are tetrahedral. The configuration being realized by coordination of the pyridine nitrogen of the two organic ligand molecules and two chloride anions.

The results of antimicrobial investigations indicate that the most active compounds are copper(II) and cobalt(II) complexes. On comparing the biological activity of the ligand and its complexes, it was found that some complexes are more effective against the bacteria. From the results, it can be concluded that nickel(II) does not increase the general antibacterial activity of the organic ligand.

The higher activity of the some complexes, as compared to the free ligands, can be understood in terms of the chelation theory. This theory explains that a decrease in the polarizability of the metal could enhance the lipophilicity of the complexes.

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