APTEFF, 33, 1–174 (2002)

UDC 661.12 : 615.281 : 54.06
BIBLID: 1450–7188, (2002) 33, pp. 151–157
Original scientific paper

SYNTHESIS, PHYSICO-CHEMICAL CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF COPPER(II) AND NICKEL(II) COMPLEXES WITH 1-BENZOYL-2-METHYLBENZIMIDAZOLE DERIVATIVES

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Chlorides of copper(II)) and nickel(II) react with 1-benzyol-2-methylbenzimidazole or 1-(4-chlorobenzoyl)-2-methylbenzimidazole to give complexes of the type $[M(L)_nCl_n(H2O)_n \cdot Cln$ *(M = Cu or Ni; L = (1-benzoyl-2-methylbenzimidazole or 1-(4--chlorobenzoyl)-2-methylbenzimidazole; n=0, 1 or 2). The complexes were synthesized and characterized by elemental analysis, molar conductivity, magnetic susceptibility measurements and IR spectra. These studies suggest that all the complexes possess an octahedral stereochemistry. The antibacterial activity of (1-benzoyl-2-methylbenz-imidazole or 1-(4-chlorobenzoyl)-2-methylbenzimidazole and their complexes was evaluated against Escherichia coli and Bacillus sp.*

KEY WORDS: benzimidazole, complexes, copper(II), nickel(II), physico-chemical characterization, biological activity

INTRODUCTION

Benzimidazole derivatives with methyl and chloro substituents in different positions have been found to possess inhibitory effect on the development of several yeasts and bacteria (1-5). Various benzimidazoles are effective inhibitors of the growth of lactobacilli, vaccinia virus, influenza virus and HIV-virus. Many different benzimidazoles have such activities as analgetics, anticarcinogens, sedatives, etc (1-8).

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The coordination chemistry of benzimidazole and its derivatives has received considerable attention because of their biological significance and interesting spectral, magnetic and structural aspects. In view of previous observations (2, 9, 10) that the presence of metal ions considerably enhances the biological activity of organic molecules, we report the synthesis and study of copper(II) and nickel(II) complexes with 1-benzoyl-2-methylbenzimidazole derivatives. The antibacterial activity of these complexes have also been investigated and is found to be in complete agreement with their structures.

EXPERIMENTAL

Reagents

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 2.5 mmol $CuCl_2 \times 2H_2O$ or $NiCl_2 \times 6H_2O$ in 10 cm^3 of EtOH was added to a solution of 5 mmol of the ligand (1-benzoyl-2-methylbenzimidazole(L^1) or 1-(4-chlorobenzoyl)-2-methyl-benzimidazole(L^2)) in 10 cm^3 EtOH. The resulting mixture was boiled under reflux on a water bath for about 2 h and then cooled. The complexes were separated from the reaction mixture by filtration, washed with EtOH and dried *in vacuo* over $CaCl_2$.

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 conductivies of freshly prepared 1×10^{-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.

Antibacterial 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 (1 cm^3) were homogenized in the tubes with 9 cm^3 of melted (45°C) nutrient agar (NA). The homogenous suspension was poured into Petri dishes.

The discs of filter paper (diameter 5 mm) were ranged on cool. After cooling on the formed solid medium, 2×10^{-5} dm^3 of the investigated compounds were placed with micropipette. After incubation for 24 hours in a thermostat at 25-27 °C, inhibition (sterile) zone diameters (including disc) were measured and expressed in mm. Inhibition

zone diameter over 8 mm indicates the tested compound is active against bacteria under investigation. Every test was done in three replications.

The antibacterial activities of the investigated compounds were tested against two strains of bacteria (*Escherichia coli* and *Bacillus sp.*). In parallel with antibacterial investigations of Cu(II) and Ni(II) complexes, all ligands were tested too, as well as the pure solvent. The concentration of each solution was 5×10^{-2} mol dm^{-3}. Commercial DMF was employed to dissolve the tested samples.

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	Colour	μ_{eff} (μ_B)	λ_M^*	Metal Found (Calcd.) %
$[Cu(L^1)_2(H_2O)Cl]Cl$	yellow	1.98	89.6	10.47 (10.17)
$[Cu(L^2)_2Cl_2]$	yellow	1.81	80.2	9.40 (9.40)
$[Ni(L^1)_2Cl_2]$	yellow-green	3.18	86.2	9.55 (9.76)
$[Ni(L^2)_2Cl_2]$	yellow-green	3.21	88.7	8.89 (8.75)

* In DMF, 1 mmol dm^{-3} solution at 25° C; in S cm^2 mol^{-1}

All the complexes are insoluble or 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 $MCl_2 \times nH_2O$ (M=Cu or Ni; n=2 or 6) with L^1 or L^2 in a mole ratio 1 : 2. It should be noticed that the reaction of the both metal ions yielded bis(ligand) complexes.

The molar conductances of copper(II)complexes in DMFsolutions fall in the range of 65-90 Scm^2mol^{-1}, corresponding to a 1:1 type of electrolyte (9). It indicates that in the case of $[Cu(L^2)_2Cl_2]$ one of the coordinated chloride ions has been replaced by DMF molecule. The molar conductance values of nickel(II) complexes are also characteristic for 1:1 types of electrolytes, which suggests a partial substitution of the coordinated chloride with solvent molecules.

Magnetic properties

Both nickel(II) complexes had μ_{eff} values in the range of 2.80-3.20 μ_B, characteristic of the octahedral nickel(II). The room temperature effective magnetic moments of the copper(II) complexes are in the range which also support their octahedral geometry (10,11).

Infrared spectra

The infrared spectra of the ligand exhibit a band at 3300-3100cm^{-1}, assigned to ν(NH). The lowering of this band frequency is due to association through the intermolecular hydrogen bonding. A sharp band observed at 1671-1660cm^{-1} is assigned to the ν(C=O) and a band at 1630cm^{-1} is assigned to the ν(C=N) oscillations in the benzimidazole ring (12).

The infrared spectra of the investigated complexes are similar to those of the corresponding ligands. The ν(C=O) absorption is shifted to lower frequences compared to the free ligands in all the complexes. This suggests coordination of the carbonyl oxygen. The ν(C=N) of the benzimidazole ring is lowered by about 15-25cm^{-1} compared to the free ligand positions. These shifts of ν(C=N) band in the IR spectra of the complexes as compared to its value in the free ligand, suggest coordination through the pyridine nitrogen of the benzimidazole to the metal ion (12). The band due to ν(NH) is shifted to lower frequences by 5-15 cm^{-1} in the complexes compared to the free ligands, and this shift is due to the formal positive charge on the secondary nitrogen when the tertiary nitrogen is coordinated.

The presented results (molar conductivities, magnetic moments and IR spectra) suggest that the Cu(II) and Ni(II) complexes have an octahedral configuration, which is realized by coordination of the two organic ligand molecules through the pyridine nitrogen and the carbonyl oxygen and chloride anions. In the case of $[Cu(L^1)_2(H_2O)Cl]Cl$ this configuration is realized by the participation of the nitrogen and oxygen of the organic ligand molecules, chloride anions and a molecule of water.

Antibacterial investigations

The antibacterial activity of these complexes was tested against phytopathogenic strains of bacteria in order to obtain new potent formulations for plant protection. All the complexes were screened for their antibacterial activities against *Escherichia coli* and *Bacilus sp.* The relevant data are presented in Table 2.

Table 2. Antibacterial activity of the benzimidazole derivatives and their complexes

Compound	*Escherichia coli*	*Bacillus sp.*
L^1	++	Ø
$[Cu(L^1)_2(H_2O)Cl]Cl$	+++	Ø
$[Ni(L^1)_2Cl_2]$	+	Ø
L^2	++	+
$[Cu(L^2)_2Cl_2]$	+++	+
$[Ni(L^2)_2Cl_2]$	+	+

Ø – no activity
\+ – low inhibitory activity
++ – medium inhibitory activity
+++ – high inhibitory activity

It is evident that both of the ligands are active against *Escherichia coli*. In the case of the *Bacillus sp.* ligand L^1 is not active. Of the complexes, the most active compounds are those containing copper(II). On comparing the biological activity of the ligand and its complexes, it was found that the copper(II) complexes are more effective against bacteria. This may be attributed to the high biological activity of free copper(II) ions.

CONCLUSIONS

(1-benzoyl-2-methylbenzimidazole and 1-(4-chlorobenzoyl)-2-methylbenzimidazole with copper(II) and nickel(II) formed complexes of the general formula $[M(L)_nCl_n(H_2O)_n]Cl_n$ (M=Cu or Ni; L = (1-benzoyl-2-methylbenzimidazole or 1-(4-chlorobenzoyl)-2-methyl-benzimidazole; n=0, 1 or 2). All the complexes are octahedral. The configuration being realized by coordination of the pyridine nitrogen and carbonyle oxygen of the two organic ligand molecules, chloride anions and molecules of water. The results of anti-bacterial investigations indicate that both of the ligands are active against *Escherichia coli*. In the case of the *Bacillus sp.* ligand L^1 is not active. Of the complexes, the most active compounds are those containing copper(II). On comparing the biological activity of the ligand and its complexes, it was found that the copper(II) complexes are more effective against the bacteria. This may be attributed to the high biological activity of free copper(II) ions.

ACKNOWLEDGMENT

These results are the part of the project "Physico-chemical, structural and biological investigations of complex compounds", supported by The Ministry for Science and Technologies of the Republic of Serbia.

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СИНТЕЗА, ФИЗИЧКО-ХЕМИЈСКА КАРАКТЕРИЗАЦИЈА И БИОЛОШКА АКТИВНОСТ БАКАР(II) И НИКАЛ(II) КОМПЛЕКСА СА ДЕРИВАТИМА 1-БЕНЗОИЛ-2-МЕТИЛБЕНЗИМИДАЗОЛА

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Хлориди бакра(II) и никла(II) реагују са 1-бензоил-2-метилбензимидазолом дајући комплексе типа $[M(L)_nCl_n(H_2O)_n]\cdot Cl_n$ (M=Cu or Ni; L=1-бензоил-2-метил-бензимидазол или 1-(4-хлоробензоил)-2-метилбензимидазол; n=0, 1 or 2). Комплекси су синтетисани и окарактерисани елементарном анализом, магнетним и кондуктометријским мерењима и IR спектрима. За све комплексе претпостављена је октаедарска структура. Испитана је антибактеријска активност 1-бензоил-2-метил-бензимидазола и 1-(4-хлоробензоил)-2-метилбензимидазола као и његових комплекса на бактерије *Escherichia coli* и *Bacillus sp.*

Received 20 May 2002
Accepted 20 September 2002