

SYNTHESIS AND ANTI *PSEUDOMONAS AERUGINOSA* ACTIVITY OF METAL COMPLEXES OF OXIME, SEMICARBAZONE AND PHENYLHYDRAZONE

Majed M. Hania

Chemistry Department, the Islamic University, Gaza, P.O.Box - 108 Gaza, (Palestine)

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ABSTRACT

Co, Ni and Cu complexes have been prepared by reacting metal chloride with the ligands of 2-formylpyridine oxime, 2-formylpyridine semicarbazone and 2-formylpyridine phenylhydrazone 1:2, and their antibacterial activity have been studied and compared with their ligands against *P. aeruginosa* which gave significant results of activity.

Key words: *Pseudomonas aeruginosa*, metal complexes, Phenylhydrazone.

INTRODUCTION

Synthesis of various heterocyclic Oxime, Semicarbazone, Phenyl hydrazone and their complexes with different transition metals are reported in the literature¹⁻⁴, and found to be active as antibacterial¹⁻⁵, antitubercular⁶, antilepral⁷, antiviral⁸, antimalarial⁹ and active against certain kinds of tumours^{10, 11}. Considering the importance of such complexes and in continuation of our earlier work^{3,4}, on transition metal complexes with oxime, semicarbazone, and phenylhydrazone derivatives, in the present communication, synthesis, characterization and antibacterial activity of Co(II), Ni(II) and Cu(II) complexes with the ligands 2-formylpyridine oxime, 2-formylpyridine semicarbazone and 2-formylpyridine phenylhydrazone are reported. The aim of this work is to study the difference in antibacterial activity between the ligands and complexes without any focusing on the structure of the complexes.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr on perkin-Elmer 883 spectrometer. All compounds gave satisfactory analysis.

2-Formylpyridine, cobalt chloride, nickel chloride, and copper chloride were obtained from sigma-Aldrich Ltd. and used without further purification.

All compounds were tested for their antibacterial activity against negative bacteria *Pseudomonas aeruginosa* at a concentration of 50 mg/disc using cup-plate method¹².

Preparation of 2-formylpyridine oxime (1)

2-formylpyridine (0.02 mol) in (15ml) ethanol was added to Aqueous solution of hydroxylamine hydrochloride (0.08 mol) and sodium acetate (0.1 mol), the mixture was heated at 80-90 °C for 10 minutes And then left to cool the precipitate was collected and purified by crystallization from ethanol to give 93 % yield ..

Preparation of 2-formylpyridine semicarbazone (2)

2-formylpyridine (0.02 mol) in (15ml) ethanol was added to aqueous solution of semicarbazide hydrochloride (0.01 mol) and sodium acetate (0.1 mol); the mixture was shaken for a few minutes And then left to precipitate and was collected, and purified by crystallization from ethanol to give 92 % yield .

Preparation of 2-formylpyridine phenylhydrazone (3)

2-formylpyridine (0.02 mol) in (15ml) ethanol was added to aqueous solution of phenylhydrazine hydrochloride (0.03mol) and sodium acetate (0.1 mol); the mixture was heated at 80-90 °C for 4h. and then left to cool. The precipitate was collected and purified by crystallization from ethanol to give 94% yield.

Complexes of 2-formylpyridine oxime with Co (II), Ni (II) and Cu (II) (1a, 1b, 1c)

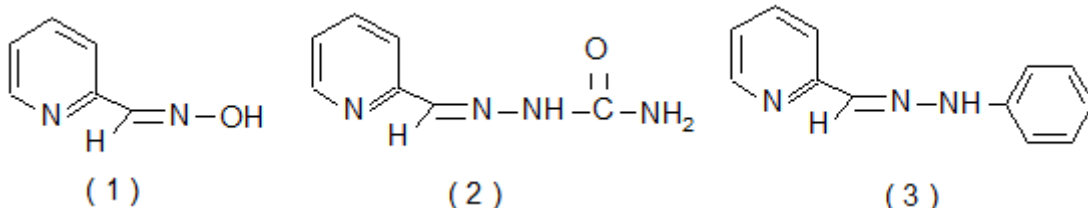
2- Formylpyridine oxime (0.02 mol) was dissolved in 15 ml ethanol and was added to dissolved cobalt, nickel and copper chloride (0.01 mol) in 15 ml ethanol. The mixture was heated at 60 °C for 2 h and then left to cool. The precipitate was collected and purified by crystallization from ethanol yield (86%, 81% and 82% respectively).

Complexes of 2-formylpyridine semicarbazone with Co (II), Ni (II) and Cu (II) (2a, 2b, 2c)

2- Formylpyridine semicarbazone (0.02 mol) was dissolved in 15 ml ethanol and was added to dissolved cobalt, nickel and copper chloride (0.01mol) in 15 ml ethanol. The mixture was heated at 60 °C for 2 h and then left to cool. The precipitate was collected and purified by crystallization from ethanol yield (87%, 83% and 85% respectively).

Complexes of 2-formylpyridine phenylhydrazone with Co (II), Ni (II) and Cu (II) (3a, 3b, 3c)

2- Formylpyridine semicarbazone (0.02 mol) was dissolved in 15 ml ethanol and was added to dissolved cobalt, nickel and cobalt copper chloride (0.01mol) in 15 ml ethanol. The mixture was stirred for few minutes then the precipitate was collected and purified by crystallization from ethanol yield (82%, 83% and 85% respectively).



RESULTS AND DISCUSSION

Oximes (1), Semicabazones (2) and phenylhydrazones (3) were prepared from 2-formylpyridine which gave white, brown and yellow a crystalline yield respectively.

All compounds are stable at room temperature and insoluble in water. Some physical properties, analytical and spectral data of the compounds are summarized in Table -1.

The infrared spectrum of free ligand (1) shows broad band at 3284 cm⁻¹, which correspond to ν (O-H) of oxime. The IR spectra of all the complexes (1a, 1b and 1c) show downshift in ν (O-H) of oxime by about 51-86 cm⁻¹. This may be due to coordinate bond formation through oxygen of

hydroxyl group¹³. The infrared spectrum of ligand (1) shows a band at ca. 1680 cm⁻¹, which may be due to ν (C=N) of oxime. The IR spectra of all the complexes show down shift ν (C = N) of oxime By about 80-86. This also may be due to coordinate bond formation through nitrogen of oximino group¹⁴. The IR spectrum of ligand shows a band of ca. 1154 cm⁻¹, which may be due to δ (N-O) of oximino group. The infrared spectra of all complexes show ν (N-O) of oximino group in the region 1133-1149 cm⁻¹.

The IR spectrum of ligand (2) shows a band at 3349 cm⁻¹ and 3405cm⁻¹ which can be assigned to ν (N-H) of amino and imino groups according to literature¹⁵. The spectra of all the complexes show these bands without almost any change. This clearly indicating the non-involvement of nitrogen atom of the mentioned groups in the coordination with metal ion.

The spectrum of ligands (2) also shows a sharp and strong band at 1680 cm^{-1} which can be assigned to $\nu(\text{C}=\text{O})$ ¹⁶. In the spectra of the complexes, this band has downshift to the $1660\text{--}1689\text{ cm}^{-1}$. This clearly indicating the involvement of oxygen atom of the carbonyl group in the coordination with metal ion.

The next IR band of structural significance in the spectra of the ligand appears at 1680 cm^{-1} . This band can be assigned to the $\nu(\text{C}=\text{N})$ group. This band has also downshift to the $1598\text{--}1605\text{ cm}^{-1}$ and clearly indicates the coordination of nitrogen to the metal ion.

Table - 1: Analytical and spectral data of compounds

Compound No.	Compounds Colour	m.p. °C	IR band cm^{-1}
1.	White	97-99	$1680\text{ }\nu(\text{C}=\text{N})$, $3284\text{ }\nu(\text{O}-\text{H})$, $1154\text{ }\nu(\text{N}-\text{O})$
2.	Yellow	198-200	$1680\text{ }\nu(\text{C}=\text{N})$, $3349\text{ }\nu(\text{N}-\text{H})$, $1690\text{ }\nu(\text{C}-\text{O})$
3.	Brown	168-170	$1680\text{ }\nu(\text{C}=\text{N})$, $3428\text{ }\nu(\text{N}-\text{H})$
1a	Black	over 300	$1605\text{ }\nu(\text{C}=\text{N})$, $3164\text{ }\nu(\text{O}-\text{H})$, $1149\text{ }\nu(\text{N}-\text{O})$
1b	Brown	218-220	$1600\text{ }\nu(\text{C}=\text{N})$, $3233\text{ }\nu(\text{O}-\text{H})$, $1134\text{ }\nu(\text{N}-\text{O})$
1c	Green	246-248	$1605\text{ }\nu(\text{C}=\text{N})$, $3198\text{ }\nu(\text{O}-\text{H})$, $1133\text{ }\nu(\text{N}-\text{O})$
2a	Blue	180-180	$1598\text{ }\nu(\text{C}=\text{N})$, $3344\text{ }\nu(\text{N}-\text{H})$, $1660\text{ }\nu(\text{C}=\text{O})$
2b	Green	170-172	$1604\text{ }\nu(\text{C}=\text{N})$, $3296\text{ }\nu(\text{N}-\text{H})$, $1668\text{ }\nu(\text{C}=\text{O})$
2c	Dark brown	over 300	$1605\text{ }\nu(\text{C}=\text{N})$, $3313\text{ }\nu(\text{N}-\text{H})$, $1689\text{ }\nu(\text{C}=\text{O})$
3a	Red	190-192	$1600\text{ }\nu(\text{C}=\text{N})$, $3175\text{ }\nu(\text{N}-\text{H})$
3b	Blue	128-130	$1600\text{ }\nu(\text{C}=\text{N})$, $3170\text{ }\nu(\text{N}-\text{H})$
3c	Green	95-97	$1607\text{ }\nu(\text{C}=\text{N})$, $3312\text{ }\nu(\text{N}-\text{H})$

Table - 2: Antibacterial activity of compounds

Compound	Antibacterial Activity
2-formyl pyridine oxime	+Ve
2-formyl pyridine Semicarbazone	-Ve
2-formyl pyridine Phenylhydrazone	-Ve
2-formyl pyridine Oxime Complex with Cobalt	+Ve
2-formyl pyridine Oxime Complex with Nickel	+Ve
2-formyl pyridine Oxime Complex with Copper	+Ve
2-formyl pyridine Semicarbazone Complex with Cobalt	+Ve
2-formyl pyridine Semicarbazone Complex with Nickel	+Ve
2-formyl pyridine Semicarbazone Complex with Copper	+Ve
2-formyl pyridine Phenylhydrazone Complex with Cobalt	+Ve
2-formyl pyridine Phenylhydrazone Complex with Nickel	+Ve
2-formyl pyridine Phenylhydrazone Complex with Copper	+Ve

The IR spectrum of ligand (3) shows a broad band at 3428 cm^{-1} which can be assigned to ν (N-H) group. This band has also downshift to the $3170\text{-}3312\text{ cm}^{-1}$ and clearly indicates the coordination of nitrogen to the metal ion. The next IR band of structural significance in the spectra of the ligand appears at 1680 cm^{-1} . This band can be assigned to the $\nu(\text{C}=\text{N})$ group. This band has also downshift to the $1600\text{-}1607\text{ cm}^{-1}$ and clearly indicates the coordination of nitrogen to the metal ion. On the basis of the above discussions, it's clear that the complexation of the free ligands and the transition metals have been formed.

Oxime (1) was found to possess moderate antibacterial activity while semicarbazone (2) and phenyl hydrazone (3) gave poor antibacterial activity. A comparative study of the ligand and its complexes as antibacterial active, indicates that the metal complexes are more active than the free ligands (2 and 3) Table -2. The increase in antibacterial activity is due to faster diffusion of metal complexes as a whole through the cell membrane or due to the combined activity effect of ligand and metal¹⁷. Such increased activity of the metal chelates can be explained as polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with electron releasing groups. It's obvious that the reducing the

total electron density on free ligands make the diffusion faster through the bacteria cell.

Conclusion

Oxime (1), semicarbazone (2) and phenyl hydrazone(3) have been synthesized from 2-formylpyridine and used as ligands in formation of complexes of Co, Ni and Cu, which show satisfactory antibacterial activity against –ve *P. aeruginosa* in case of oxime (1), but poor antibacterial activity against –ve *P. aeruginosa* in case of semicarbazone (2) and phenylhydrazone (3). This might come from the difference in total electron density between the mentioned compounds. By means that semicarbazone (2) and phenylhydrazone (3) have higher electron density than oxime (1), which prevent the inhabitation throw the body of the bacteria. All complexes of oxime (1), semicarbazone (2) and phenyl hydrazone (3) gave good antibacterial activity against –ve *P. aeruginosa*, this come from the decreasing of electron density on the ligands in complexes. This means that “the higher electron density compound the lower antibacterial active”.

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