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Synthesis and Antibacterial Activity of Some Transition Metal Complexes of Oxime, Semicarbazone and Phenylhydrazone

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

Key Words: Synthesis, Transition metal complexes, Oxime, Semicarbazone, Phenylhydrazone, Antibacterial activity.

INTRODUCTION

Metal complexes with ligands containing nitrogen and sulphur donor atoms have been found useful as potential drugs[1-5] and fungicidal agents[6,7]. Synthesis of various heterocyclic oximes, semicarbazones, phenyl hydrazones and their complexes with different transition metals are reported in the literature[8-15] and found to be active as antibacterial[8-14], antitubercular[15], antilepral[16], antiviral[17], antimalarial[18] and active against certain kinds of tumours[19,20]. Considering the importance of such transition metal complexes and in continuation of our earlier work[10,13], on transition metal complexes with oxime, semicarbazone, and phenylhydrazone derivatives, in the present paper, synthesis, characterization and antibacterial activity of Co(II), Ni(II) and Cu(II) complexes with 2-formylthiophene oxime, 2-formylthiophene semicarbazone and 2-formylthiophene phenylhydrazone are reported.

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-Formylthiophene, 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 μg/disc using cup-plate method[21].

Preparation of 2-formylthiophene oxime (1): 2-Formylthiophene (0.004 mol) in (15 mL) ethanol was added to aqueous solution of hydroxylamine hydrochloride (0.06 mol) and sodium acetate (2 g), the mixture was warmed for 10 min and then left to cool the precipitate was collected and purified by crystallization from ethanol to give 90 % yield.

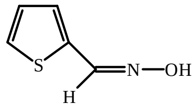
Preparation of 2-formylthiophene semicarbazone (2): 2-Formylthiophene (0.015 mol) in (15 mL) ethanol was added to aqueous solution of semicarbazide hydrochloride (0.025 mol) and sodium acetate (3 g); the mixture was shaken for a few minutes and then left to precipitate and was collected, and purified by crystallization from ethanol to give 87% yield.

Preparation of 2-formylthiophene phenylhydrazone (3): 2-Formylthiophene (0.007 mol) in (15 mL) ethanol was added to aqueous solution of phenylhydrazine hydrochloride (0.01 mol) and sodium acetate (1.5 g), the mixture was warmed for 15 min and then left to cool. The precipitate was collected and purified by crystallization from ethanol to give 92 % yield.

Complexes of 2-formylthiophene oxime with Co(II), Ni(II) and Cu(II) (1a-c): 2-Formylthiophene oxime (0.002 mol) was dissolved in 15 mL ethanol and was added to dissolved cobalt, nickel and copper chloride (0.001 mol) in 15 mL ethanol. The reaction mixture was stirred on a magnetic shaker. The precipitate was collected and purified by crystallization from ethanol yield (74, 71 and 76 %, respectively).

Complexes of 2-formylthiophene semicarbazone with Co(II), Ni(II) and Cu(II) (2a-c): 2-Formylthiophene semicarbazone (0.002 mol) was dissolved in 15 mL ethanol and was added to dissolved cobalt, nickel and copper chloride (0.001 mol) in 15 mL ethanol to give precipitate. The precipitate was collected and purified by crystallization from ethanol yield (67, 81 and 73 %, respectively).

Complexes of 2-formylthiophene phenylhydrazone with Co(II), Ni(II) and Cu(II) (3a-c): 2-Formylthiophene semicarbazone (0.002 mol) was dissolved in 15 mL ethanol and was added to dissolved cobalt, nickel and copper chloride (0.001mol) in 15 mL ethanol. The mixture was stirred for few minutes then the precipitate was collected and purified by crystallization from ethanol yield (74, 79 and 69 %, respectively).



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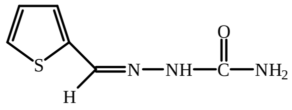

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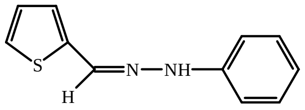

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RESULTS AND DISCUSSION

Oxime (**1**), semicabazone (**2**) and phenylhydrazone (**3**) were prepared from 2-formylthiophene which gave white, white 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.

TABLE-1
ANALYTICAL AND SPECTRAL DATA OF COMPOUNDS

Compounds No.	Colour	m.p. (^{o}C)	Key IR band (cm^{-1})
1	White	141-143	1633 ν (C=N), 3200 ν (O-H), 1141 ν (N-O)
2	White	224-226	1620 ν (C=N), 3320 ν (N-H), 1650ν (C=O)
3	Yellow	120-122	1675 ν (C=N), 3420 ν (N-H)
1a	Red	187-189	1585 ν (C=N), 3190ν (O-H), 1085 ν (N-O)
1b	Green	243-245	1595 ν (C=N), 3115 ν (O-H), 1081 ν (N-O)
1c	Brown	162-164	1605 ν (C=N), 3150 ν (O-H) 1074 ν (N-O)
2a	White	230-232	1514 ν (C=N), 3164 ν (N-H) 1600 ν (C=O)
2b	White	237-239	1604 ν (C=N), 3230 ν (N-H) 1672 ν (C=O)
2c	Dark Brown	172-174	1599 ν (C=N), 3162ν (N-H) 1688 ν (C=O)
3a	Black	207-209	1595ν (C=N), 3302ν (N-H)
3b	Black	202-204	1610ν (C=N), 3152ν (N-H)
3c	Green	< 300	1620ν (C=N), 3260ν (N-H)

The infrared spectra of free ligand (**1**) shows broad band at 3200 cm^{-1}, which correspond to ν(O-H) of oxime. The IR spectra of all the complexes (**1a**-**c**) show downshift in ν(O-H) of oxime by about 10-75cm^{-1}. This may be due to coordinate bond formation through oxygen of hydroxyl group[22]. The infrared spectrum of ligand (**1**) shows a band at *ca.* 1633 cm^{-1}, which may be due to ν(C=N) of oxime. IR spectra of all the complexes show down shift ν(C=N) of oxime by 28-48 cm^{-1}. This may also be due to coordinate bond formation through nitrogen of oximino group[23]. IR spectra of ligand shows a band at 1141 cm^{-1}, which may be due to ν(N-O) of oximino group. The infrared spectra of all complexes show ν(N-O) of oximino group in the region 1085-1074 cm^{-1}.

IR spectra of ligand (**2**) shows a band at 3320 cm^{-1} which can be assigned to ν(N-H) of imino group[24]. The spectra of all the complexes show down shift ν(N-H) of imino group to the 3230-3162 cm^{-1}.The spectra of ligands (**2**) also shows a sharp and strong band at 1650 cm^{-1} which can be assigned to ν(C=O)[25]. In the spectra of the complexes, this band has downshift to the 1688-1600 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 1620 cm^{-1}. This band can be assigned to the ν(C=N) group. This band has also downshift to the 1604-1514 cm^{-1} and clearly indicates the coordination of nitrogen to the metal ion.

IR spectra of ligand (**3**) shows a broad band at 3420 cm^{-1} which can be assigned to ν(N-H) group. This band has also downshift to the 3302-3152 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 1675 cm^{-1}. This band can be assigned to the ν(C=N) group. This band has also downshift to the 1620-1595 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 phenylhydrazone (**3**) gave poor antibacterial activity This means that the mesomeric effect present in semicarbazones and Phenyl hydrazones more significant than in case of oximes, which makes the diffusion of these compounds more difficult throw the body of the bacteria[26].

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).

TABLE-2
ANTIBACTERIAL ACTIVITY OF COMPOUNDS

Antibacterial activity	Compounds	Antibacterial activity	Compounds
+ ve	2-Formylthiophene oxime	+ ve	2-Formylthiophene semicarbazone complex with cobalt
- ve	2-Formylthiophene semicarbazone	+ ve	2-Formylthiophene semicarbazone complex with nickel
- ve	2-Formylthiophene phenylhydrazone	+ ve	2-Formylthiophene semicarbazone complex with copper
+ ve	2-Formylthiophene oxime complex with cobalt	+ ve	2-Formylthiophene phenylhydrazone complex with cobalt

Antibacterial activity	Compounds	Antibacterial activity	Compounds
+ ve	2-Formylthiophene oxime complex with nickel	+ ve	2-Formylthiophene phenylhydrazone complex with nickel
+ ve	2-Formylthiophene oxime complex with copper	+ ve	2-Formylthiophene phenylhydrazone complex with copper

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 metal[27]. 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 is 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-formylthiophene 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 prevents 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 have been supported our earlier work, by means that the higher electron density compound the lower antibacterial active.

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