

Synthesis, characterisation and microbial studies of nickel (II) complexes derived from N-amidino-N¹-naphthylthiourea

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ABSTRACT

Some novel metal complexes of nickel (II) derived from N-amidino-N¹-naphthylthiourea (NPTU) have been synthesized and characterized by elemental analysis, molar conductance and spectral studies. The ligand behaves as neutral bidentate and coordinates through sulphur and nitrogen. Complexes are ascertained the general formula $[\text{Ni}(\text{NPTU})_2\text{X}_2]$ ($\text{X} = \text{Cl}^-$, Br^- , ClO_4^- , NO_3^- , NCS^-). Thermal behaviour of $[\text{Ni}(\text{NPTU})_2(\text{NO}_3)_2]$ was determined. Ligand and metal complexes were screened for their antibacterial and antitubercular activities.

Key words: Nickel(II) complexes, N-amidino-N¹-naphthylthiourea, antibacterial activity, antitubercular activity, thermal study.

INTRODUCTION

Amidinothiourea and its derivatives are found to be excellent industrial and biological molecule. Recently research work on safe accelerators are has gained interest worldwide that amidinothiourea derivative, are found to be non toxic and it is used in many pharmaceutical applications¹. Amidinothiourea and its derivatives processes several potential coordinating modes since it can act as an N, N or S, N-ligand due to thiol-thioketo tautomerism. Transition metal complexes have attracted great interest for their application in industrial and biological fields.

In the present study, we report the preparation, characterization and antimicrobial activity of nickel(II) with an amidinothiourea derivative viz, N-amidino-N¹-naphthylthiourea (NPTU) Fig.1.

EXPERIMENTAL

All the chemicals used were of Analar Grade, obtained from commercial suppliers, Fluka/Sisco Research Laboratories (India).

The preparation of the ligand N-amidino-N¹-naphthylthiourea (NPTU) Fig. 1. consists of 2 stages. First stage is the preparation of phenyl isothiocyanate, which was prepared by standard procedure². Liquor ammonia (115ml) was taken in a R. B. flask and carbondisulphide (55 ml) was added slowly. Aniline (60 ml) was added little by little, shaking the mixture throughout. Yellow crystalline product formed was filtered, dissolved in water (100 ml) and steam distilled with lead nitrate (200 gm) dissolved in water (400 ml) for 3 hrs. The yellow oily liquid formed was extracted with ether. In the second stage guanidine hydrochloride (0.1 mol) and sodiumhydroxide (0.1 mol) were take in acetonitrile (25 ml) to which phenyl isothiocyanate (0.1 mol) was added drop wise with constant stirring for about 2 hrs. It was diluted with water and precipitated solid was collected, recrystallised from hot water, dried and kept over anhydrous calcium chloride. The yield was about 78-80%.

The nickel (II) complexes of NPTU were prepared by the following general method. An ethanolic or methanolic solution of the metal salt was added to a hot solution of NPTU in the same solvent. The metal salt to ligand molar ratio was

kept as maintaining the ligand in slight excess. The contents were refluxed in a water bath for about 2 hrs. complex separated was cooled, filtered, washed with ethanol and dried over anhydrous calcium chloride.

The elemental analysis of the complexes were determined by LECOCHN 600 Elemental Analyser. Nickel (II) ion in the metal complexes were estimated complex metrically with EDTA using murexide and erichrome black – T as indicators after decomposing the complex with nitric acid and a few drops of bromine water. The halogens and thiocyanate were estimated by Volhard's method and perchlorate by KURZ's method³. The molar conductance measurements were carried out using 10^{-3} M solutions of the complexes were carried out using KBr disc on a Shimadzu 8201 PC FT Infrared Spectrophotometer and electronic spectra were recorded on a Hitachi 320 UV-Visible spectrophotometer. The thermogravimetric analysis was carried out using a thermo balance of type Mettler Toledo STARe system. The room temperature magnetic moment measurements were made using a Guoy magnetic valence and the diamagnetic corrections for various atoms and structural units were computed from Pascal's constants⁴.

Microbial activity of the ligand and metal complexes were assessed against *E. coli*, *S. aureus* and *M. Tuberculosis* by resazurin assay method⁵. The bacterial culture was grown till their mid-log phase in the appropriate media (LB broth for *E. coli*, nutrient broth for *S. aureus* and middle brook 7H9 broth for *M. tuberculosis* H 37 Rv). From this, fifty microliters of the culture were added to 450 μ l fresh medium in 2 ml micro centrifuge tubes. The test solution (complexes) were prepared at a stock concentration of 2 mg/ml in DMF. The drugs were tested in 10 μ g/ml and 100 μ g/ml concentrations. Control tubes had the same volumes of medium, bacterial culture and DMF without any drug. All the samples were taken in duplicates. The tubes were then kept for incubation at 37°C for 7 days. After incubation 20 μ l of 0.01% resazurin (Sigma, St. Louis, MO. USA) in water was added to each tube. The control tubes showed change of colour from blue to pink after 24 hrs. at 37°C. The complexes which prevented the change of colour of the dye

were considered to be inhibitory to the microbes.

RESULTS AND DISCUSSION

All the newly synthesized complexes are fairly stable at room temperature and possess good keeping qualities. They are non-hygroscopic solids moderately soluble in methanol, ethanol, chloroform and dimethylsulphoxide. Molar conductivities of all the complexes are found to be in the range corresponding to that of non-electrolytes. Analytical data of the complexes are represented in (Table 1).

The IR spectrum of the ligand shows a number of strong and weak bands in the region 3400-3100 cm^{-1} . The bands are assigned to N-H stretching vibrations⁶. A strong band at 1630 cm^{-1} is assigned to $\nu_{(\text{C}=\text{N})}$ and characteristic bands at 1490, 1300 and 950 cm^{-1} are due to NCS frequencies. The band at 890 cm^{-1} is attributed to $\nu_{(\text{C}=\text{S})}$. In the complexes the absorption bands due to $\nu_{(\text{C}=\text{N})}$ of the ligand is shifted to lower frequencies. The $\nu_{3(\text{NCS})}$ band at 950 cm^{-1} of the ligand is considerably shifted to higher frequencies and the $\nu_{(\text{C}=\text{S})}$ band at 890 cm^{-1} is observed at lower frequencies in the complexes. The observations show that S and N atoms of the ligand are coordinated to the metal. Moreover the additional band at 550 cm^{-1} in the complexes is characteristic of M-N coordination⁷.

The occurrence of two strong bands in the nitrate complex around 1520 cm^{-1} and 1430 cm^{-1} are attributed to ν_4 and ν_1 modes of vibrations of nitrate ion. The absence of ν_2 band around 1000 cm^{-1} shows that no ionic nitrate is present. Since the frequency separation ($\nu_4 - \nu_1$) is in the range 100-200 cm^{-1} is reasonable to infer that the nitrate group is coordinated monodentately⁸. The N-coordinated nature of thiocyanate⁹ is indicated by $\nu_{\text{C-N}}$ at 2070 cm^{-1} , $\nu_{\text{C-S}}$ at 830 cm^{-1} and δ NCS near 490 cm^{-1} . In the perchlorate complex there are three additional bands at 1100 cm^{-1} , 1080 cm^{-1} and 630 cm^{-1} . These are assigned to ν_4 , ν_1 and ν_3 vibrations of perchlorate ion. The split nature of ν_4 and ν_1 bands indicates that the perchlorate ion is coordinated unidentately¹⁰. The molar conductance value also supports uncoordinated nature of nitrate, perchlorate and N-coordinated nature of thiocyanate in the

Table 1: Analytical, conductivity and magnetic moment data of the complexes

Complexes	Yield%	Analytical data (%) [*]						Molar conductance ($\Omega^{-1} \text{ cm}^{-2} \text{ mol}^{-1}$)		Magnetic moment BM
		M	C	H	N	S	DMF	Methanol		
$[\text{Ni}(\text{NPTU})_2\text{Cl}_2]$	72	9.38 (9.52)	46.79 (46.77)	3.54 (3.60)	18.24 (18.18)	10.31 (10.40)	15.84	22	2.91	
$(\text{Ni}(\text{NPTU})_2\text{Br}_2)$	74	58.19 (8.32)	4.82 (40.87)	3.04 (3.15)	15.73 (15.89)	9.03 (9.09)	14.62	24	2.93	
$[\text{Ni}(\text{NPTU})_2(\text{NO}_3)_2]$	73	8.54 (8.76)	34.59 (34.75)	2.73 (2.67)	20.78 (20.92)	9.39 (9.58)	16.18	19	3.04	
$[\text{Ni}(\text{NPTU})_2(\text{NCS})_2]$	72	8.63 (8.87)	47.18 (47.20)	3.38 (3.35)	21.23 (21.17)	19.43 (19.39)	18.21	23	3.06	
$[\text{Ni}(\text{NPTU})_2(\text{ClO}_4)_2]$	71	7.89 (7.88)	38.43 (38.72)	3.01 (2.98)	15.15 (15.05)	8.59 (8.61)	14.83	25	2.88	

^{*} Calculated values are given in parentheses.

respective complexes. The non-ligand bands appearing in the far IR around 320 cm^{-1} and 290 cm^{-1} for the chloro and bromo complexes are assignable $\nu(\text{M}-\text{Cl})$ and $\nu(\text{M}-\text{Br})$ stretching vibrations.

The newly synthesized complexes exhibit a broad absorption around $24390\text{-}23800 \text{ cm}^{-1}$ which is assignable to $n \rightarrow \pi^*$ transition of the ligand molecule. There are two very weak absorption bands are present around $20830\text{-}20480 \text{ cm}^{-1}$ and $17240\text{-}16671 \text{ cm}^{-1}$ in the spectra of the complexes. These bands can be assigned to ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g} (\text{p})$ and ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g} (\text{F})$ transition of an octahedrally coordinated nickel(II) ion¹¹. The μ_{eff} values of the NPTU complexes of nickel(II) are in the range $2.9\text{!}3.06 \text{ BM}$. These values are in the range expected for an octahedral nickel(II) complexes¹².

The complex $[\text{Ni}(\text{NPTU})_2(\text{NO}_3)_2]$ was subjected to thermogravimetric analysis in dynamic air at a heating rate of $10^\circ\text{C}/\text{min}$. The complex undergoes a two stage decomposition as indicated by the DTG peak. A plateau upto 170°C in the TG curve indicate that the complex is stable up to this temperature and the absence of coordinated water or other solvent molecules¹³. The first stage decomposition beings at 300°C and gets completed at 420°C with a peak temperature at 345°C . The second stage decomposition begins at 580°C and ends at 660°C with a peak temperature 611°C , which corresponds to the formation of metal oxide. The formation of the final residue is substantiated by the agreeable results obtained from the mass loss data of TG.

On the basis of all the above spectral data and physicochemical studies it is clear that all the complexes are neutral and associated with two molecules of the ligand in coordination sphere and the structure shown in Fig. 2 may be assigned to these complexes.

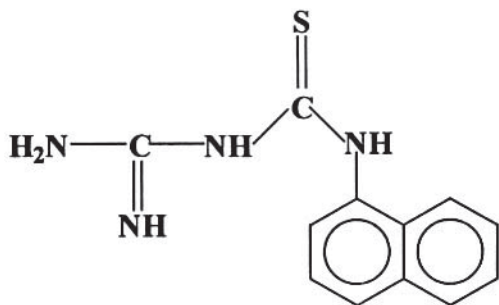
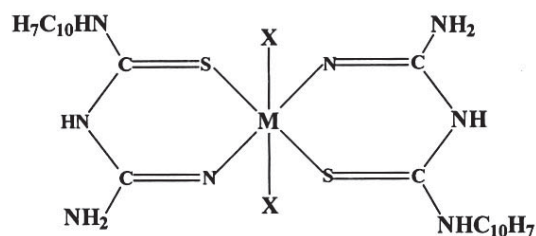
The ligand and the metal complexes were screened fro their antibacterial activity by resazurin assay method. Resazurin in an oxidation reduction indicator used for the evaluation of cell growth. It is a blue on fluorescent and non-toxic dye that becomes pink and fluorescent when reduced to resorufin by oxidoreductases with in viable cells. The

Table 2: Antitubercular activity of the ligand and metal complexes

Complex	Con.µg/ml	Activity against		
		<i>E. coli</i>	<i>S. aureus</i>	<i>M. tuberculosis</i>
NPTU	10	-	-	-
	100	-	-	-
[Ni(NPTU) ₂ Cl ₂]	10	-	-	-
	100	+	-	+
(Ni(NPTU) ₂ Br ₂]	10	-	-	-
	100	-	+	+
[Ni(NPTU) ₂ (NO ₃) ₂]	10	-	-	-
	100	-	-	+
[Ni(NPTU) ₂ (NCS) ₂]	10	-	-	-
	100	+	+	+
[Ni(NPTU) ₂ (ClO ₄) ₂]	10	-	-	+
	100	+	+	+

results obtained are presented in (Table 2). The increases activity of the metal chelates than the ligand can be explained on the basis of Overton's concept and Tweedy's chelation theory¹⁴. On chelation the polarity of the metal ion will be reduced to a greater extent due to the overlap of the positive charge of the metal with the donor groups. Further, it increases the delocalisation of pi-electrons over the whole chelate ring and hence enhance the liposolubility of the complexes. This increased liposolubility enhances the penetration of the

complexes into the lipid membrane. From the result it is clear that ligand shows negative activity against the microbis. All the complexes are active against M-tuberculosis in 100 µg concentrations. The chloro and thiocyanato complexes are more active than nitrate complexes. This is because the bonding capacity of nitrate ion-towards the central metal ion is greater than that of the chloride ion and the extend of metal ion available is lessened for the display of antibacterial activity.

**Fig. 1: Structure of ligand**

M = Ni and X = Cl⁻, Br⁻, ClO₄⁻, NO₃⁻, NCS⁻

Fig. 2: Structure of metal complexes

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