

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NIOBIUM (V) COMPLEXES OF COUMARIN BASED IMINES

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ABSTRACT

The reactions of niobium pentaisopropoxide with monofunctional bidentate Schiff bases, 3-acetyl-coumarin-hydrazinecarboxamide and 3-acetyl coumarin hydrazinecarbothioamide have been carried out in different molar ratios. The resulting new derivatives are coloured solids and nonelectrolytes in nature. On the basis of IR, ¹HNMR and electronic spectral data along with their magnetic susceptibilities probable structures have been assigned to these complexes.

Keywords: Niobium (V) complexes, 3-acetyl-coumarin, semicarbazone, thiosemicarbazone, antibacterial and antifungal activity.

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INTRODUCTION

A few Schiff base derivatives¹⁻² of some of the V group elements have been described in the literature. Recently, the synthesis of several new derivatives of niobium with bifunctional tridentate Schiff bases has been reported from these laboratories³⁻⁵. However, reactions of niobium pentaisopropoxide with monobasic bidentate imines do not seem to have been investigated earlier. Metal-chelated Schiff base complexes have continued to play the role of one of the most important stereochemical models in main group and transition-metal coordination chemistry due to their preparative accessibility, diversity and structural variability⁶⁻⁷. Schiff bases are an important class of compounds in the medicinal and pharmaceutical fields. Coordination complexes of sulfur and nitrogen donors have been widely investigated and show novel structural features⁸, unusual spectral and catalytic properties⁹, and relevance to biological systems¹⁰. The present paper describes the synthesis and characterization of two new biologically potent imines and their niobium (V) complexes.

EXPERIMENTAL

Materials and Methods

All the chemicals used were of B.D.H. grade and dried by the standard methods. Benzene (B.D.H.) was dried over sodium wire and finally by distilling azeotropically with ethanol. Isopropanol (B.D.H.) was refluxed over sodium and then distilled over aluminium isopropoxide. Niobium pentaisopropoxide was prepared by the ammonia method¹¹ by the reaction of anhydrous pentachloride with isopropanol and distilled before use. The imines were prepared by the usual condensation method and then recrystallised¹². All glass apparatus fitted with quickfit interchangeable joints and protected with calcium chloride guard tubes was used. The fractionations were carried out on a column packed with Raschig rings and fitted to a ratiohead with condenser.

Niobium was determined as niobium pentaoxide and nitrogen by Kjeldahl's method. Sulfur was estimated by Messenger's method. Carbon and hydrogen analysis of the complexes as well as the ligands were performed at the Micro Analytical Laboratory of the Department of Chemistry, Punjab University, Chandigarh. Isopropanol was estimated by oxidation with a standard potassium dichromate solution in 12.5% sulphuric acid¹³. Molecular weights were determined by Rast Camphor Method. Conductance

measurements were recorded on Century Digital Conductivity Meter Model CC601 at room temperature. UV Spectra were recorded on a varian-cary/5E Spectrophotometer at SAIF,IIT Madras, Chennai. IR spectra were recorded on a Perkin-Elmer Model 577 Grating Spectrophotometer in the range 4000-200 cm^{-1} in KBr optics as well as in Nujol mulls. ^1H NMR spectra were recorded on a JEOL-AL-300 FTNMR Spectrometer in DMSO-d_6 using TMS as the internal standard.

Preparation of the imines (LH)

The imines 3-acetyl-coumarin-hydrazinecarboxamide (L^1H) and 3-acetyl coumarin hydrazinecarbothioamide (L^2H) were prepared by the condensation of 3-acetyl-2H-chromen-2-one with semicarbazide hydrochloride (in presence of sodium acetate) and thiosemicarbazide respectively in equimolar ratio (1:1) in ethanol. The contents were refluxed for about 3-4 hours in thermal method. These were purified by recrystallization in the same solvent and dried. Their structures have been shown in Figures-1 and 2.

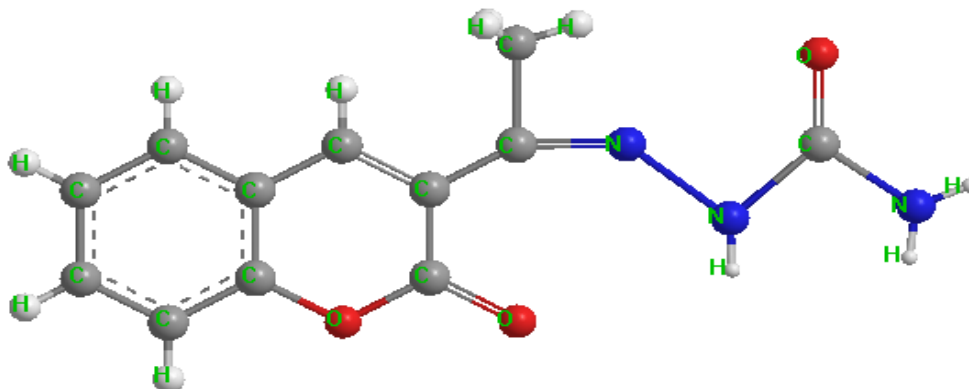


Fig.-1: 3-Acetyl-coumarin-hydrazinecarboxamide(L^1H)

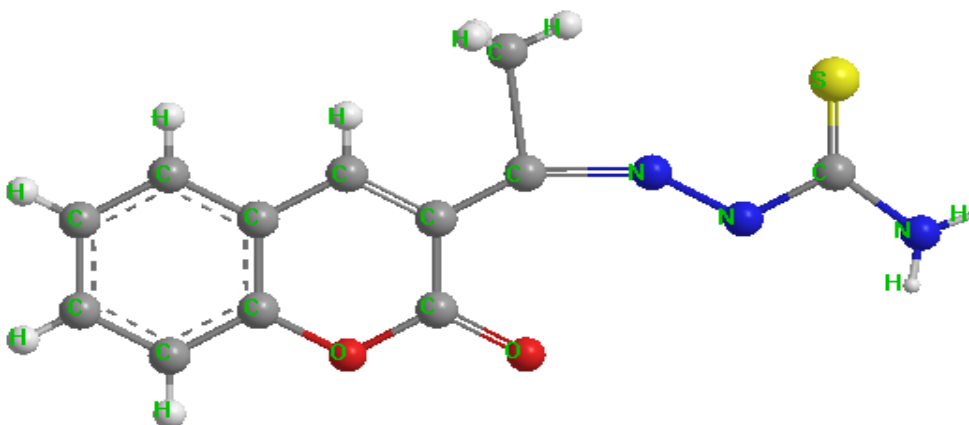


Fig.-2: 3-Acetyl coumarin hydrazinecarbothioamide (L^2H)

Synthesis of Niobium (V) imine complexes

Niobium pentaisopropoxide and the imines (L^1H) and (L^2H) were taken in anhydrous benzene. The contents were refluxed under an efficient fractionating column for 12-14 hours on an oil bath at 120-125°C. When the boiling point attained the temperature of benzene (80°C), the heating was stopped and the excess of the solvent was removed under reduce pressure. The resulting new derivatives were obtained in almost theoretical yields and their physical properties and analytical data are presented in Table-1.

Table-1: Physical Properties of Nb(V) Complexes and Ligands

S.No.	Ligands and their complexes	Colour and state	M.P. (°C)	Mol.Wt Found (Calcd)	C Found (Calcd)	H Found (Calcd)	N Found (Calcd)	S Found (Calcd)	Nb Found (Calcd)
1	C ₁₂ H ₁₁ N ₃ O ₃ (L ¹ H)	Cream	195	244.23 (245.23)	58.12 (58.77)	4.22 (4.52)	17.10 (17.13)	-	-
2	C ₂₄ H ₃₈ N ₃ NbO ₇	Cream	222-228	572.12 (573.18)	49.91 (50.26)	6.19 (6.68)	6.56 (7.33)	-	15.99 (16.20)
3	C ₃₄ H ₄₄ N ₆ O ₉ Nb	Pale Yellow	225-230	770.56 (773.22)	52.12 (52.78)	4.17 (5.73)	9.56 (10.86)	-	11.13 (12.01)
4	C ₄₄ H ₅₀ N ₉ O ₁₁ Nb	Off white	230-235	970.56 (973.27)	53.12 (54.27)	5.00 (5.18)	11.56 (12.94)	-	8.13 (9.54)
5	C ₁₂ H ₁₁ N ₃ O ₂ S(L ² H)	Yellow	215	261.16 (261.30)	55.09 (55.16)	4.11 (4.24)	16.00 (16.08)	12.13 (12.27)	-
6	C ₂₄ H ₃₈ N ₃ NbO ₆ S	Dark yellow	215-220	636.56 (637.23)	47.91 (48.89)	5.99 (6.50)	6.86 (7.13)	4.65 (5.44)	14.99 (15.76)
7	C ₃₄ H ₄₄ N ₆ O ₇ S ₂ Nb	Orange	235-240	804.23 (805.79)	50.60 (50.89)	7.49 (5.50)	11.16 (11.53)	6.25 (7.96)	10.56 (11.53)
8	C ₄₄ H ₅₀ N ₉ O ₈ S ₃ Nb	Dark Brown	232-237	1020.00 (1021.2)	50.60 (51.71)	4.49 (4.93)	11.16 (12.33)	6.25 (9.41)	9.00 (9.09)

Biological Activity

Antifungal activity

The antifungal activity¹⁴ of the prepared imines and their Nb (V) complexes were tested by Radial Growth Method¹⁵ against the pathogenic fungi *Rhizoctinia Solani*, *Penicillium Chrysogenum*, *Rhizopus oryzae* and *Aspergillus flavus*. (Graph-1)

Radial Growth Method

Potato dextrose agar medium was prepared in the flask and then sterilized. The principle involved in this method is to "poison" the nutrient medium with a fungitoxicant (compound) and then allowing a test fungus to grow on such medium. The fungi were grown in potato-dextrose agar medium (glucose – 20 g, starch – 20 g, agar-agar – 20 g and 1000 mL of water) and the requisite amount of compounds was dissolved in methanol to obtain different concentrations (100 and 200 ppm). The medium was then poured into Petri plates and small disc (0.7 cm) of the fungus culture was cut into a sterile cork borer and transferred aseptically in the centre of a Petri dish containing the medium with a certain amount of the compound. Suitable checks were kept where the culture discs were grown under the same conditions on PDA without the compound. These Petri dishes were wrapped in polythene bags containing a few drops of alcohol and were placed in an incubator at $25 \pm 2^\circ\text{C}$. Three replicates were used in each case. The colony diameter, after 96 hours was compared with the check. The linear growth of the fungus was obtained by measuring the diameter of the colony in Petri plates and the percentage inhibition was calculated by the following formula-

$$\% \text{ Inhibition} = 100 (C - T) / C$$

Where, C = diameter of the fungal colony in check/control plate

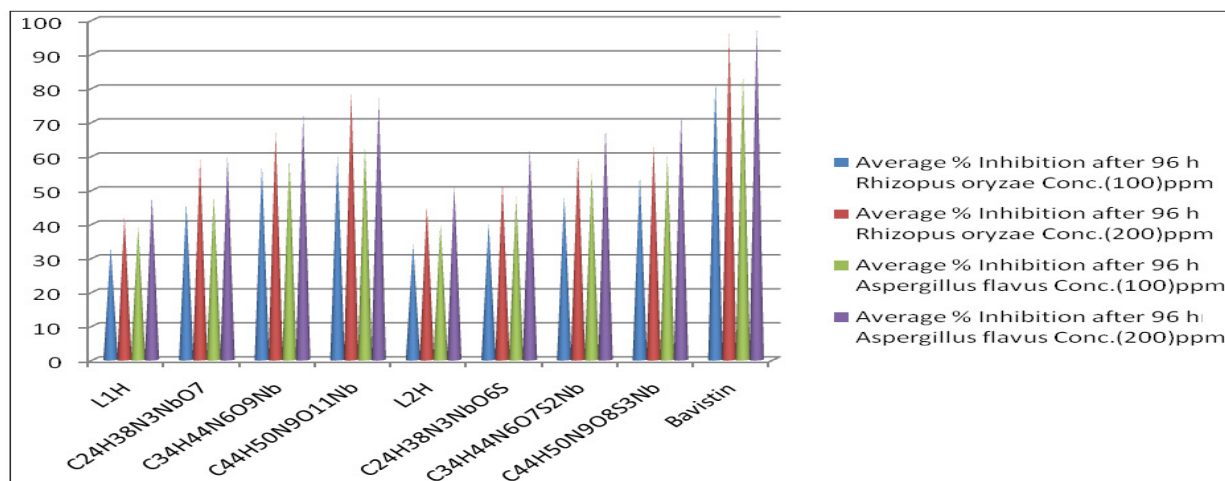
T = diameter of the fungal colony in test plate.

The results were compared with the standard fungicide (Bavistin). The antifungal activity of the imines and their niobium complexes has been shown in Graph-1.

Antibacterial Activity

Antibacterial activity¹⁶ was evaluated against *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* by the "paper disc plate method" using inhibition zone technique. The agar medium having the composition peptone(5g), beef extract (5g), NaCl (5g), agar-agar (20g) and

distilled water 1000 mL and 5mm diameter paper discs of Whatman No. 1 were used¹⁷. The agar medium was poured in petri plates. The solution of the test compound in methanol in 500 and 1000 ppm concentration were prepared, and either the discs were dipped in solution of the test sample and placed on seeded plates, or the required quantity of the test sample was pipetted on the disc. The petri plates having these discs on the seeded agar should first be placed at low temperature for 2 hours to allow for the diffusion of a chemical before being incubated at suitable optimum temperature $25 \pm 2^\circ\text{C}$ for 20- 30 hours. The results of these findings have been shown in Graph-2.



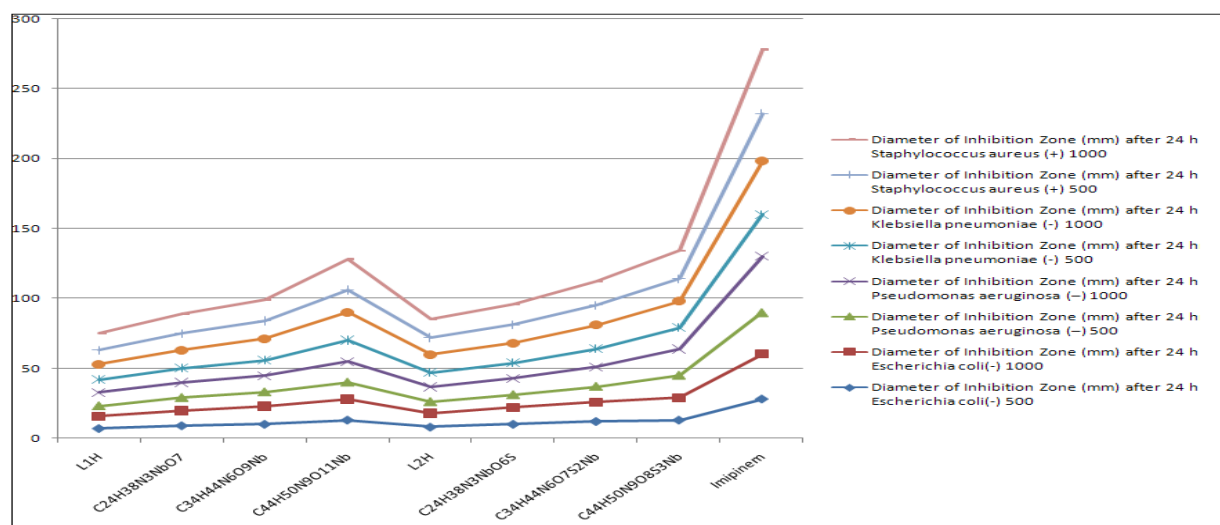
Graph-1 : Antifungal screening of L^1H , L^2H and their Nb(V) complexes

RESULTS AND DISCUSSION

The reactions of niobium pentaisopropoxides with the monobasic bidentate imines (LH) in 1:1, 1:2 and 1:3 molar ratios can be represented by the following general equations-



(Where M= Nb and LH is monobasic bidentate imines)



Graph-2: Antibacterial activity of L^1H , L^2H and their Nb(V) complexes

The reactions have been found to be quite facile and could be completed on 10-15 hours of refluxing. The progress as well as the completion could be monitored by estimating the liberated isopropanol in the binary azeotrope with benzene oxidimetrically.

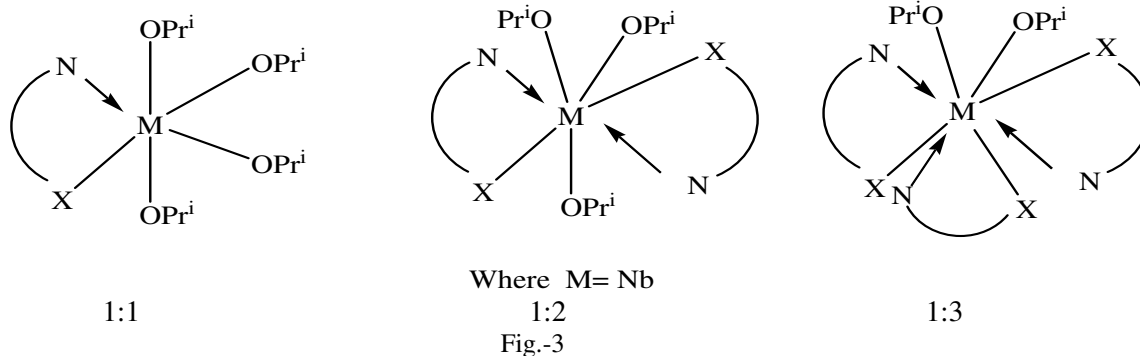
The resulting complexes are moisture-sensitive, obtained as coloured solids and are soluble in most of the common organic solvents such as benzene, chloroform, dimethylformamide, dimethylsulfoxide, methanol and acetone. The cryoscopic determination of molecular weights in benzene shows the monomeric nature of these complexes, thus indicating coordination numbers six, seven and eight in mono, di and tri substituted derivatives respectively, as shown in Fig.-3.

Conductance Measurements

The low value of molar conductivity ($10\text{--}15 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$) of the resulting complexes in anhydrous DMF shows them to be non-electrolytes in nature.

Magnetic susceptibilities

The magnetic susceptibilities of the compounds were also determined at $30 \pm 0.1^\circ\text{C}$. The complexes are diamagnetic in character as the specific susceptibilities ($\chi_s \times 10^6 \text{ c.g.s.}$) of these complexes lie in the range -0.41 to -0.73 .



Spectral Studies

Electronic Spectra

The electronic spectra of the ligands recorded in methanol display two maxima at ~ 276 and $\sim 326 \text{ nm}$ which are due to $\pi\text{--}\pi^*$ electronic transitions and remain almost unchanged in the spectra of the metal complexes. The band around 370 nm is due to the $n\text{--}\pi^*$ transitions of the $>\text{C}=\text{N}$ chromophore and shows a bathochromic shift of $20\text{--}30 \text{ nm}$ after the coordination of the azomethine nitrogen to the metal atom, indicating the delocalization of the electronic charge within the chelate ring and thereby stabilizing the resulting complexes.

IR Spectra

The IR spectra of the free imines L^1H and L^2H have absorption bands at $3150\text{--}3250$, $1600\text{--}1610$ and $1080/1690 \text{ cm}^{-1}$ are assigned to $-(\text{NH})$, $(>\text{C}=\text{N})$ ¹⁸, and $(>\text{C}=\text{S})/(>\text{C}=\text{O})$, respectively. The broad band due to $-(\text{NH})$ vibrations, disappears in the spectra of the complexes, indicating the deprotonation of this group on coordination with the metal atom. The negative shift ($10\text{--}20 \text{ cm}^{-1}$) of $(>\text{C}=\text{N})$ band observed in all the complexes indicates the involvement of azomethine nitrogen upon complexation. The bands due to $(>\text{C}=\text{S})$ and $(>\text{C}=\text{O})$ are shifted towards lower frequencies in the complexes indicating coordination of sulfur and oxygen to the central metal atom. The spectra of the free imines display two sharp bands at $3400\text{--}3500$ and $3350\text{--}3400 \text{ cm}^{-1}$ due to asym and sym vibrations of NH_2 group, respectively, which remain at almost the same positions in the spectra of the complexes, suggesting that the NH_2 group is not involved in chelation. The appearance of some new bands at 1170 , 1130 ± 5 and $1110 \pm 7 \text{ cm}^{-1}$ are due to the presence of the isopropoxy groups and bands of relatively medium intensity occurring in the regions $605\text{--}590$, $540\text{--}510$ and $380\text{--}365 \text{ cm}^{-1}$ may be attributed to the $\nu(\text{Nb}\text{--}\text{O})$ ¹⁹, $\nu(\text{Nb}\text{--}\text{N})$ ²⁰ and $\nu(\text{Nb}\text{--}\text{S})$ ²¹ respectively, in the resulting complexes. (Table-2)

Table-2: IR (cm⁻¹) and ¹H NMR (δ, ppm) Spectral Data of the Ligands and their Corresponding Complexes

Compound	IR spectral data (cm ⁻¹)				¹ H NMR spectral data (δ, ppm)			
	(>C=N)	(Nb-S)	(Nb-O)	(Nb←N)	-NH	-CH=N	-NH ₂	Aromatic protons (m)
L ¹ H	1600	-	-	-	8.69	-	3.45	6.45-8.12
C ₂₄ H ₃₈ N ₃ NbO ₇	1595	-	605	540	-	-	3.42	6.48-8.35
C ₃₄ H ₄₄ N ₆ O ₉ Nb	1590	-	600	530	-	-	3.43	6.72-8.06
C ₄₄ H ₅₀ N ₉ O ₁₁ Nb	1585		590	535			3.41	6.48-8.35
L ² H	1610	-	-	-	8.49	-	3.42	6.42-8.02
C ₂₄ H ₃₈ N ₃ NbO ₆ S	1600	380	-	535	-	-	3.40	6.76-8.06
C ₃₄ H ₄₄ N ₆ O ₇ S ₂ Nb	1605	370	-	510	-	-	3.41	6.65-8.11
C ₄₄ H ₅₀ N ₉ O ₈ S ₃ Nb	1590	365	-	530			3.42	6.48-8.35

¹H NMR Spectra

The ¹H NMR spectra of both the imines recorded in DMSO-d₆ exhibit a broad peak at δ 8.49-8.69 ppm due to -NH proton (Table-2). The -NH proton signal of the ligands disappears in the complexes. The absence of this signal in these complexes suggest that this proton has been lost via ketoenolization/thioenolization of >C=O/>C=S groups and coordination of oxygen to the metal atom, has taken place. The >CH=N proton moves downfield in the complexes in comparison with its original positions in the ligand due to coordination of >C=N to the metal atom.

Biological Assay

The antifungal and antibacterial studies show that niobium complexes have more inhibitory effect than do parent imines due to chelation²² of niobium atom with the ligand moieties. Chelation tends to make a ligand a more potent bactericidal agent. Other factors such as solubility, conductivity and dipole moment, affected by the presence of metal ion, may also increase the biological activity of the metal complexes compared to the ligand.

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