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Synthesis, Characterization and 3-D Molecular Modeling of Some Oxovanadium(IV) Complexes Involving O_2N_2 Donor Core

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ABSTRACT

Vanadium plays an important role in life and one of its most relevant properties identified is its capacity to act as insulin-enhancing agent, either in the form of its inorganic salts or complexes with organic ligands. Besides the antidiabetic action, vanadium complexes are known to possess potent anticancer activity, which deserve increasing attention for application to biomedical sciences. Synthesis and studies of Vanadium complexes have induced a considerable amount of interest due to their application as important catalysts in several chemical reactions.

In view of the wide application of Vanadium complexes, a series of oxovanadium(IV) complexes involving pyrazolone-based aroylhydrazone and 8-hydroxyquinoline have been synthesized and characterized by different physicochemical studies such as elemental analysis, molar conductance, magnetic measurements, infrared, TGA, ESR, mass and electronic spectral studies.

The overall experimental data based from all the studies presented suggests the complexes under present investigation are of the general composition [VO(L)(8-hq)(H_2O)], where LH= pyrazolone-based aroylhydrazone and 8-hqH= 8-hydroxyquinoline, involving a monobasic didentate (*O,N*) donor ligand. An octahedral structure with axial oxo groups have been proposed for these complexes.

Key words: oxovanadium(IV), 4'-benzoyl-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one derivative, salicylic acid hydrazide, benzoic acid hydrazide, hydrazine hydrate, isonicotinic acid hydrazide, 8-hydroxyquinoline.

Introduction

Vanadium is normally present at very low concentrations ($<10^{-8}$ M) in virtually all cells in plants and animals [1]. In mammals, vanadium is mainly stored in bones, liver and kidney[2-4]. It is an ultramicrotrace bioelement[5] with interesting biological properties[6-9]. Research on vanadium was stimulated by the findings of English *et al.*[10], on the role of the metal as an inhibitor of terminal differentiation of murine erythroleukemia cells and by Thompson *et al.*[11], on the inhibition, by dietary vanadyl sulfate, of chemically induced mammary carcinogenesis. The latter also, provided evidence that this trace metal may be an effective chemo preventive agent. The biological effects of vanadium compounds such as the insulin-like action[12,13] and the reduction of hyperlipidemia and hypertension, in relation to their few adverse effects[14], indicates the potential therapeutic applications of these compounds.

Acid hydrazides and hydrazones[15] are useful chelating agents and are of biological importance[16]. The hydrazone derivatives are used as fungicides and in the treatment of diseases such as tuberculosis, leprosy and mental disorders. The remarkable biological activity of acid hydrazides R-CO-NH-NH_2, their corresponding hydrazones R-CO-NH-N=CH-R' and the dependence of their mode of chelation on the transition metal ions present in the living system have offered significant interest in the recent years[17-23]. Hydrazones moieties[24] are the most important pharmacophoric cores of several anti-inflammatory, antinociceptive and antiplatelet drugs[25].

Pyrazolone derivatives are potent non-salicylate, analgesic, antipyretic, anti-inflammatory and antirheumatic agents[26]. They also show antidiabetic[27,28], anticancer[29] and antineoplastic[30] properties.

The chemistry of quinoline and its derivatives has attracted much attention because of their therapeutic properties[31,32]. Some of the derivatives are used as antiprotozoal, antifungal, antiamoebic, antiseptic drugs and also as antiperspirant.

In view of the above mentioned importance of vanadium compounds, hydrazones, pyrazolone derivative and quinoline derivative, the synthesis and characterization of some oxovanadium(IV) complexes involving O_2N_2-donor core of hydrazones of pyrazoline derivative and 8-hydroxyquinoline has been done.

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Experimental

Materials used

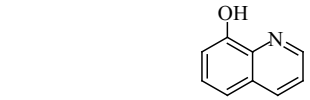
Vanadyl sulphate pentahydrate, acetylacetone and benzoyl chloride were products of Thomas Baker Ltd., Mumbai, while 8-hydroxyquinoline was purchased from E. Merck (India) Ltd., Mumbai, 3-methyl-1-phenyl-2-pyrazolin-5-one from Lancaster, England and isonicotinic acid hydrazide from Aldrich Chemical Co., U.S.A. Methyl salicylate, methyl benzoate and hydrazine hydrate were products of Sisco Chem., Mumbai. All other chemicals used were of A.R. grade.

Preparation of 4-benzoyl-3-methyl-1-phenyl-2-pyrazolin-5-one (bmphp)

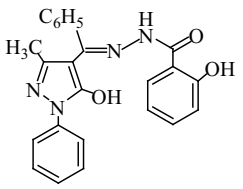
It was prepared by the Jensen's method[33] by using calcium hydroxide, 3-methyl-1-phenyl-2-pyrazolin-5-one, benzoyl chloride and DMF.

Preparation of Schiff base ligands

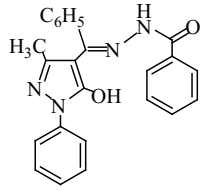
An ethanolic solution of bmphp (2 mmol) was added to the solution of 2 mmol of salicylic acid hydrazide, benzoic acid hydrazide, hydrazine hydrate or isonicotinic acid hydrazide in ethanol. The resulting mixture was refluxed with stirring for 3-4 hrs. A bright yellow or orange precipitate was formed while refluxing. It was filtered and washed several times with ethanol and dried in a desiccator over anhydrous$CaCl_2$.



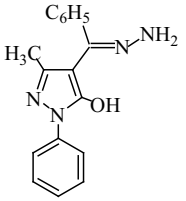
8-hqH



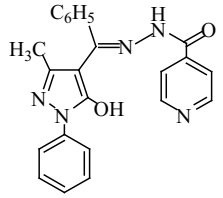
sa-bmphpH **(I)**



ba-bmphpH **(II)**



hhH-bmphpH **(III)**



ina-bmphpH **(IV)**

Synthesis of complexes

To a 1mmol of 8-hydroxyquinoline in ethanol was added 1 mmol of the Schiff base, sa-bmphpH, ba-bmphpH, hhH-bmphpH or ina-bmphpH in ethanol. The resulting mixture of the two appropriate ligands was added slowly with constant stirring to the solution of 1mmol of $[VO(acac)_2]$ in ethanol. The resulting brown solution was refluxed with stirring for 4-5 hrs. A deep green colored precipitate was formed while refluxing. The complex so obtained was suction filtered, washed several times with 1:1 ethanol-water solution and dried *in vacuo*.

$$[VO(acac)_2] + 8\text{-hqH} + LH \xrightarrow[\text{Reflux}]{\text{Ehanol, } H_2O}$$

$$\xrightarrow[\text{Reflux}]{\text{Ehanol, } H_2O} [VO(L)(8\text{-hq})(H_2O)] + 2acacH$$

Where LH= sa-bmphpH, ba-bmphpH, hhH-bmphpH or ina–bmphpH and 8-hqH = 8-hydroxyquinoline

Results and Discussion

Infrared spectral studies

The hydrazone ligands used in the present investigations were prepared by the interaction of hydrazine hydrate or acid hydrazide with 4'-benzoyl-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one derivative.

The IR spectra of all the hydrazones exhibit ν(N-H) mode normally as a broad band centered at 3133-3255 cm^{-1}. A strong band appeared in the region 1628- 1645 cm^{-1} for the ligand was assigned to ν(C=O). This suggests that the carbonyl group of the acid hydrazide moiety is in the *keto* form in the solid state. All the hydrazones exhibit a broad band centered at 3412-3432 cm^{-1}, suggesting the involvement of 5-OH group of the pyrazolone moiety in the intramolecular hydrogen bonding with the lone pair of azomethine nitrogen. The above two observations conclude the existence of the ligands in *enol* form in the solid state.

When enolic –OH group (pyrazolone moiety) is coordination to the metal center, the ν(OH) mode observed at 3412-3432 cm^{-1} should disappear in the IR spectra of the complexes under study. Unfortunately this could not be said with certainty as the complexes in question also exhibit absorption in the overlapping region (3380-3443 cm^{-1}) due to the presence of coordinated water. However the appearance of a medium intensity band at 1363-1388 cm^{-1} (with change in the nature of peak) in all the complexes compared to ν(C-O) (enolic) mode of the respective ligands appearing in the region 1352-1364 cm^{-1}. This suggests the coordination of enolic oxygen of the pyrazolone moiety after deprotonation[34].

The ligands under discussion show sharp and strong band due to ν(C=N) of the azomethine group at 1593-1616 cm^{-1}. The observed low energy shift of this band in the complexes and appearing at 1557-1593 cm^{-1} suggests the coordination of the azomethine nitrogen.

Most of the oxovanadium complexes exhibits a strong band near 1000 cm^{-1}, which has been assigned to the ν(V=O) mode[35]. In contrast several oxovanadium(IV) complexes reported in which this stretching mode appear at quite lower wave numbers around 900 cm^{-1}. The shift of ν(V=O) to lower wave numbers has been suggested due to the presence of a ----V=O----V=O---- chain structure[36], which is formed by the interaction of vanadyl oxygen of one molecule with a vanadium metal in another molecule. In the present work

ν(V=O) is found at 951-977 cm^{-1} which suggests the absence of a ----V=O----V=O---- chain structure[37-38].

The appearance of a broad band centered at 3380-3443 cm^{-1} due to ν(OH) in all the complexes may be due to the presence of coordinated water in these complexes.

The two significant absorption bands due to coordinated 8-hydroxyquinoline are ν(C=N) (ring nitrogen) and ν(C-O), and these are observed in the regions 1628-1630 cm^{-1} and 1100-1120 cm^{-1} respectively in all the complexes. These results, which are in agreement with the results reported elsewhere[39], suggest the bidentate (*N,O*) coordination of the ligands to vanadium in all the complexes.

ESR spectral studies

The X-band EPR spectrum at –196 °C of one representative compound, [VO(sa-bmphp)(8-hq)(H_2O)] **(1)** was recorded on powdered sample using microwave frequency 9.12 GHz. Unfortunately no hyperfine splitting was observed in the present case. The spectrum is similar to many other ESR spectra of powdered oxovanadium(IV) compounds[1,40-41]. The calculated value of "g" for the compound **(1)** was found to be 1.9479

The g factor is a dimensionless constant and its actual value for a free electron is 2.0036. The shifting of g value from 2.0036 towards lower side suggests the mixing of the metal orbital involved in molecular orbitals. It can be said, in other word, that the metal ligand bonds are covalent[42] and the compound is paramagnetic.

Thermogravimetric analysis

Thermogravimetric analysis of a representative compound[VO(ba-bmphp)(8-hq)(H_2O)] **(2)** was carried out in the temperature range 29 °C-1020 °C at the heating rate of 20 °C/min. The compound shows a weight loss of 3.20% at 148 °C which corresponds to the elimination of one molecule of coordinated water per molecule of the complex (calcd. 2.88%). Several weight losses shown by this compound at different temperatures could not be correlated separately. However the weight loss of 86.45% shown by this compound around 995 °C corresponds to the removal of two ligand moieties along with one molecule of coordinated H_2O (calcd. weight loss = 89.27%). The final residue (observed 13.55%) corresponds to V_2O_5 (calcd. 14.57%).

Mass spectral studies

The FAB mass spectrum of a representative ligand, ba-bmphpH **(II)** and its complex, [VO(ba-bmphp)(8-hq)(H_2O)] **(2)** were recorded on a JEOL SX 102/DA-6000 Mass Spectrometer/ Data system using Argon/ Xenon (6 KV, 10 mA) as the FAB gas. The accelerating voltage was 10 KV and the spectra were recorded at room temperature. *m*-Nitrobenzyl alcohol (NBA) was used as the matrix.

The mass spectral peak observed at 136, 154, 289 and 307 m/z are matrix peaks. The spectral peaks of the ligand **(II)** observed at 261 and 396 m/z are most probably due to the following types of fragments:

Ligand (II)

(i) $[bmphp]^+$ moiety (261) = **261**

(ii) $[ba\text{-}bmphpH]^+$ (396) = **396**

In case of the complex **(2)** the spectral peak observed at 211, 462 and 605 m/z are correlated due to the following type of ion associations:

Complex (2)

(i) $[8\text{-}hq]^+(144)+[V{=}O]^+$ (66.94) = 210.94 = ~ **211**

(ii) [molecular ion]$^+$(605.94)–$[8\text{-}hq]^+$(144)=461.94= ~ **462**

(iii) [molecular ion]$^+$ (605.94) = 605.94 = ~ **605**

These results are consistent with the proposed composition of the ligand (ba-bmphpH) and its corresponding complex [VO(ba-bmphp)(8-hq)(H_2O)].

Electronic Spectra

The electronic spectra of all the complexes were recorded in 10^{-3} M dimethylformamide. Besides high intensity charge transfer transitions, all these complexes show one low intensity d-d transition.

Magnetic Measurements

The oxovanadium(IV) is an S=½ system. The magnetically dilute oxovanadium(IV) complexes usually exhibit magnetic moments to their spin-only value (1.73 B.M.). The observed magnetic moments of the present complexes at room temperature are in the range 1.65-1.74 B.M., suggest that the complexes under this investigation are paramagnetic with respect to one unpaired electron and are mononuclear.

Conductance measurements

The observed molar conductance values of the complexes measured in 10^{-3} molar dimethylformamide solutions are in the range 20.7 – 29.1 ohm^{-1} cm^2 $mole^{-1}$, which are consistent with the non-electrolytic nature of the complexes. Such a non-zero molar conductance value for each of the complex in the present study is most probably due to the strong donor capacity of dimethylformamide, which may lead to the displacement of anionic ligand and change in electrolyte type.

Conclusion

The satisfactory analytical data coupled with the studies presented above suggest that he complexes prepared in this investigation are of the general composition [VO(L)(8-hq)(H_2O)], where LH= sa-bmphpH **(I)**, ba-bmphpH **(II)**, hhH-bmphpH **(III)** or ina–bmphpH **(IV)** and 8-hqH= 8-hydroxyquinoline. Keeping in view, the monomeric hexa-coordination of all the complexes, and the well established structure of N,N'-ethylenebis(glysino)oxovanadium(IV) involving a monobasic didentate (*O,N*) donor ligand [similar

to ligand (*O,N*)] in the present investigation, octahedral structure with axial oxo groups have been proposed for these complexes.

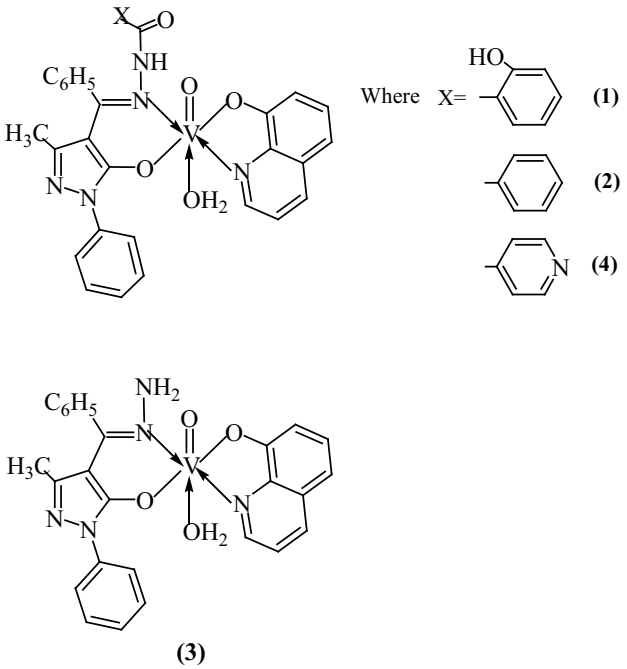


Fig. *Proposed structure of Complexes*

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