

SYNTHESIS AND STUDY OF DICARBOXALIC ACID HYDROZONE DERIVATIVE AND THEIR VANADIUM COMPLEXES

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ABSTRACT - Two novel hydrazone derivatives and their vanadium complexes have been synthesized bearing the formula $V[DPODH](BF_4)_2$ and $V[DCODH](BF_4)_2$, where $M=V$, $DPODH=2,6$ -diacetyl pyridine dichloride - $N-N'$ -Oxydiacetyl dihydrazone and $DCODH=2,6$ -pyridine diacarbonyl dichloride - $N-N'$ -Oxydiacetyl dihydrazone and $(BF_4)=$ Tetrafluoroborate. They are characterized by elemental analysis, spectral studies, conductivity measurements and magnetic measurements. The result of analysis shows the complexes to be of octahedral geometry and electrolytic nature. The biological screening of hydrazone complexes showed antimicrobial activity against three bacteria and two fungi. These observations have been guiding for the development of new hydrazones that possess varied biological activity.

Key Words: Hydrazone derivatives¹, vanadium complexes², spectral & biological studies³.

INTRODUCTION

Hydrazone compounds obtained by the reaction of aromatic and heterocyclic hydrazides with mono and di-aldehydes or ketones have revealed very versatile behavior in metal coordination [1-4]. Several coordination complexes have been synthesized and investigated during the last few decades. Ever since the importance of coordination phenomenon in biological processes was realized, many metal containing macromolecules have been synthesized and studied to understand the mechanism of complex biological reactions. The importance of coordination complexes in our day to day life is increasing due to their complex structures and interesting magnetic, electronic and optical properties. This has resulted in the emergence of an important branch of inorganic chemistry viz. bioinorganic chemistry. Coordination compounds also find extensive applications in analytical and medicinal chemistry.

EXPERIMENTAL

Materials

All the chemicals and solvents used of A.R. grade, purchased from Aldrich, Himedia, Merck and were used as received.

General procedure for the synthesis of ligand

1:2 stoichiometric quantities of transparent oxydiacetic acid ester (1.62gm, 0.01M) solution and hydrazine hydrate (0.83cm³, 0.02M) were mixed in 20ml. ethyl alcohol with continuous stirring. The obtained solution was refluxed over a water bath at 40-50°C for around 5-6 hours. Thereafter, obtained white crystal in bottom round flask was concentrated to one-third of its original volume. Then, the obtained solution was cooled overnight and white crystals were filtered, washed with alcohol and ether then dried in vacuum over anhydrous CaCl₂ in a desiccator.

Synthesis of 2,6- diacetyl pyridine dichloride - $N-N'$ - oxydiacetyl dihydrazone

1:1:1 stoichiometric quantities of oxydiacetic acid dihydrazide (1.86 gm., 0.01M), vanadium acetate (1.85 gm., 0.01M) and 2, 6-diacetyl pyridine (1.63gm., 0.01M) were mixed in 20 ml. ethanol with continuous stirring. The obtained solution was refluxed over a water-bath for around 6-7 hours. Thereafter, it was concentrated to one-third of its original volume. Then a little of sodiumtetrafluoroborate was added and the

solution was cooled overnight when metallic gray crystals separated out. The crystals were filtered, washed with alcohol and then dried in vacuum over anhydrous CaCl_2 in a desiccator.

Synthesis of 2,6- pyridine dicarbonyl dichloride -N-N'- oxydiacetyl dihydrazone

1:1:1stoichiometric quantities of oxydiacetic acid dihydrazide (1.86 gm., 0.01M), vanadium acetate (1.85 gm., 0.01M) and 2,6-pyridine dicarbonyl dichloride (1.90 gm., 0.01M) were mixed in 20ml. Ethanol with continuous stirring till white precipitate were seen on the wall of flask with white fumes. After disappearance of fumes, the solution refluxed over a water-bath for around 6-7 hours. Thereafter, it was concentrated to one-third of its original volume then a little of sodiumtetrafluoroborate was added. The solution was cooled overnight when dark-gray crystal separated out. These crystals were filtered, washed with alcohol and then dried in vacuum over anhydrous CaCl_2 in a desiccator.

ANALYTICAL AND PHYSICAL MEASUREMENTS

The elemental analysis helps in fixing the stoichiometric composition of the ligand and hydrazone derivatives and their vanadium complexes. The carbon, hydrogen, nitrogen, oxygen analyzed by sophisticated analytical instrument facility such as Elemental Analyzer (*Thermo Scientific 338 35210*) and weighing by Micro Balance (*Mettler Toledo Model XP₆*), melting point determine by (*Make-VEEGO, Model- VMP-PM*). For metal estimation, using gravimetric method of analysis *Vogel's Quantitative Inorganic Analysis (seventh edition) revised by G.SVEHLA*. Infra-red spectra of synthesized compounds were recorded on (*Perkin Elemer- Model No.- C91158*) in the range $4000\text{-}400\text{ cm}^{-1}$. The electronic spectra of complexes in DMSO were recorded on a UV-VIS-NIR (*Cary5E*) spectrophotometer at room temperature.

Table1: Elemental analysis and Molar conductivity data of the ligand and newly synthesized hydrazone derivatives and their vanadium complexes

COMPOUND	M.P. (°C)	COLOR	YIELD
ODADH	162	White	1.54 gm.
V(II)[DPODH](BF ₄) ₂	279	Metallic-Grey	1.98 gm.
V(II)[DCODH](BF ₄) ₂	283	Dark-Grey	1.89 gm.

COMPOUND	ELEMENTAL ANALYSIS (%) (F/c)				MOLAR CONDUCTIVITY (ohm ⁻¹ cm ² mol ⁻¹)
	C	H	N	M	
ODADH	29.60 (29.63)	6.16 (6.22)	34.54 (34.55)	-	-
V(II)[DPODH](BF ₄) ₂	30.24 (30.27)	3.29 (3.32)	13.57 (13.58)	9.77 (9.88)	113.24
V(II)[DCODH](BF ₄) ₂	23.71 (23.73)	1.97 (1.99)	12.57 (12.58)	9.10 (9.15)	113.17

INFRA-RED DATA

The band due to the $-\text{NH}_2$ group disappeared completely in the complexes. The band due to the $-\text{NH}$ group did not show any change in the spectra of complexes, confirming that the Nitrogen of $-\text{NH}$ group did not take part in reaction whereas a sharp band was seen in the range of 1320cm^{-1} proving that $-\text{NH}_2$ group is present in the ligand. Some entirely new absorption band appeared in the spectra of complexes viz. band

around 520–510cm⁻¹ due to M–N group, a band around 430–410cm⁻¹ due to M–O group. These new band confirmed the coordination of nitrogen and oxygen with the metal atom in the complexes.

Figure 1: Infra-red spectrum of ligand ODADH

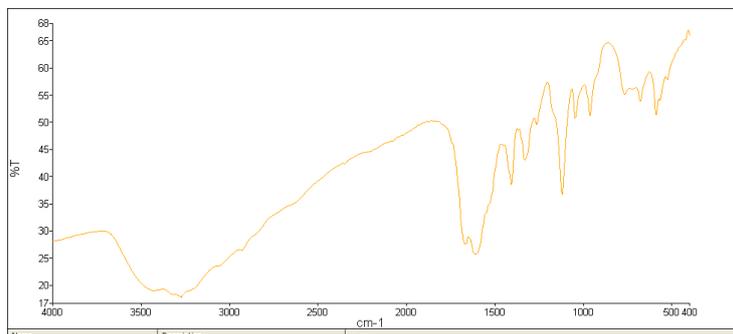


Figure 2: Infra-red spectrum synthesized complexes of V(II)[DPODH](BF₄)₂

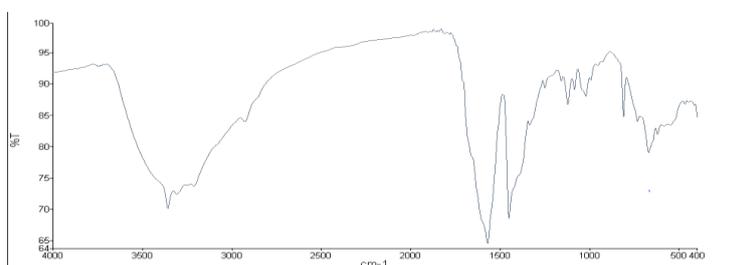


Figure 3: Infra-red spectrum synthesized complexes of V(II)[DCODH](BF₄)₂

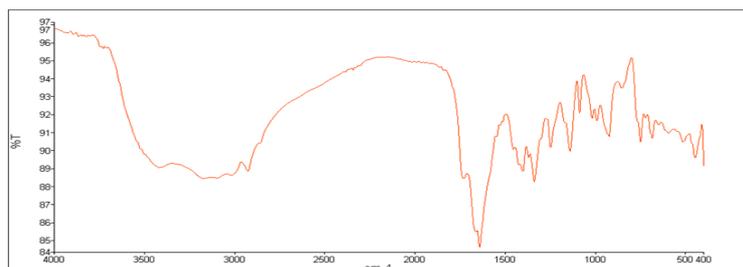


Table : 2 Infra-red spectral data of ligand and newly synthesized hydrazone derivatives and their vanadium complexes

S. NO.	FUNCTIONAL GROUPS	ODADH	V(II)[DPODH](BF ₄) ₂	V(II)[DCODH](BF ₄) ₂
1.	-CH ₂	2820	2790	2780
2.	-NH ₂	1320	-	-
3.	-NH	3365	3360	3360
4.	N-N	910	890	870
5.	>C=N	-	1540	1530
6.	>C=O	1670	1640	1630
7.	M-N	-	510	520
8.	M-O	-	430	410

ELECTRONIC DATA

The synthesized hydrazone derivatives and their vanadium complexes are stable in air, completely insoluble in water and common organic solvents, but they are soluble in DMSO. The electronic spectra of the complexes recorded in DMSO (HPLC grade). All the absorption bands in electronic spectra were found for complexes in the range of 11,850-11,700 cm^{-1} attributed to ${}^2E_g \rightarrow {}^2T_{2g}$ transition and in the range of 23,450–23,400 cm^{-1} attributed to L→M charge transfer transition. These transition confirmed the octahedral geometric of the complexes.

Table : 3 Absorption bands (in cm^{-1}) of hydrazone derivatives and their vanadium complexes

S. NO.	COMPLEXES	TRANSITION (cm^{-1})	
		${}^2E_g \rightarrow {}^2T_{2g}$	L→M
1.	V(II)[DPODH](BF ₄) ₂	11850	23450
2.	V(II)[DCODH](BF ₄) ₂	11700	23400

MINIMUM INHIBITORY CONCENTRATION (MIC)

The MIC values determine by the sets to of “two fold serial dilution method”. In this method 1 ml. of seeded broth (obtained by 1:100 dilution of the indicated micro-organism in broth) was taken in ten well sterilized tubes (3x100mm. size) keeping the first test tube empty 2ml. of each of the seeded broth was prepared having 100 $\mu\text{g/ml}$. and test compound in two tubes. A and B respectively (prepared by dissolving 0.2 ml. and 0.3 ml. of the stock solutions (1 $\mu\text{g/ml}$.) in 1.8 ml. and 1.7 ml of broth respectively). Contents of the tube A were placed in the first empty tube using a fresh sterilized pipette. 1 ml. contents from the B tube were withdrawn and added to second tube and mixed well. Similarly, 1 ml. contents from the first tube were withdrawn and added into the third tube and mixed well. 1ml. contents from the third tube were pipette out with other fresh sterilized pipette and added into fourth tube and shaken well. This gradient dilution process was continued for all the ten test tubes using a fresh pipette each time. 1ml. contents were taken out from the tenth tube and rejected. All the test tubes were labeled with 100 $\mu\text{g/ml}$., 75 $\mu\text{g/ml}$., 50 $\mu\text{g/ml}$., 25 $\mu\text{g/ml}$., 12.5 $\mu\text{g/ml}$., 6.25 $\mu\text{g/ml}$., 3.125 $\mu\text{g/ml}$., 1.562 $\mu\text{g/ml}$., 0.78 $\mu\text{g/ml}$. and 0.39 $\mu\text{g/ml}$. respectively. 1ml. of each of the seeded broth and broth was placed in two separate tubes for the control of culture and control of broth media respectively in each set of above experiments simultaneously. All the above sets of tubes were incubated in BOD incubator for the respective indicated micro-organisms. The tube having the highest dilution showing no visible turbidity was chosen. The amount of the test compound in this tube was the minimum inhibitory concentration.

Figure : 4 Antimicrobial property determination of micro-organism in Mueller Hinton Agar (Well Method)

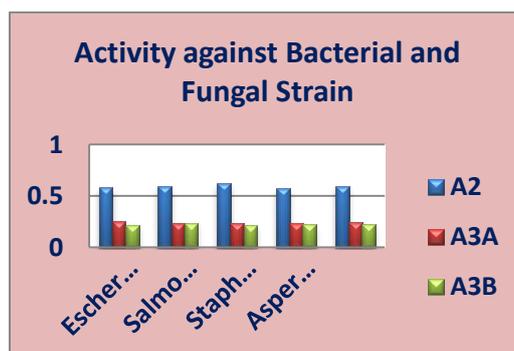


Table: 4 Minimum Inhibitory Concentration (MIC) in molar Concⁿ. [X10⁻⁴] of ligand and newly synthesized hydrazone derivatives and their vanadium complexes

Compounds	Activity against bacterial strain		
	<i>E. coli</i> (Gram-Negative)	<i>Salmonella</i> (Gram-Negative)	<i>Staphylococcus aureus</i> (Gram-Positive)
ODADH	0.585	0.595	0.624
V(II)[DPODH](BF ₄) ₂	0.250	0.236	0.235
V(II)[DCODH](BF ₄) ₂	0.220	0.231	0.220

Compounds	Activity against fungal strain	
	<i>Aspergillus brasiliensis</i>	<i>Candida albicans</i>
ODADH	0.575	0.591
V(II)[DPODH](BF ₄) ₂	0.235	0.245
V(II)[DCODH](BF ₄) ₂	0.223	0.225

Figure: 5 Activity against bacterial and fungal strain



RESULTS AND DISCUSSION

Both the hydrazone derivatives and their vanadium complexes are solid and colored. Complexes which are stable at room temperature. The ligand and hydrazone derivatives and their vanadium complexes are white-metallic grey and dark-grey in color and they are soluble in DMSO and DMF. All compounds give satisfactory elemental analyses results as are shown in the Table-1. In infra-red spectral data in Figure-1, 2 & 3 and in Table-2, nitrogen, oxygen suitably placed for coordination towards the metal ion, has been proposed for all the synthesized complexes, whereas absent in ligand confirm an octahedral geometry of complex I and complex II. Electronic spectral data of ligand and hydrazone derivatives and their vanadium complexes are shown in Table-3. The molar conductance range indicates the complexes electrolytic nature and indicating 1:1:1: stoichiometric for complexes ligand confirms an octahedral geometry of complex I and complex II. Electronic spectral data of ligand and hydrazone derivatives and their vanadium complexes are shown in Table-3. The Minimum inhibitory concentration (MIC) value in molar concⁿ are shown in Figure- 4&5 and in Table-4 of ligand and complexes compared whereas complexes showed good antimicrobial activities than ligand.

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