SYNTHESIS, SPECTRAL AND BIOLOGICAL ACTIVITIES OF PYRIDINE 2,6 DICARBOXALIC ACID HYDRAZONE DERIVATIVES AND ITS METAL COMPLEXES

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Abstract: The new series of two new hydrazone derivatives and their vanadium complexes have been synthesized bearing the formula $M[DPDH](BF_4)_2$ and $M[DCDH](BF_4)_2$, where M=V, DPDH= (2,6-diacetylpyridine-N,N'-Pyridine-2,6-dicarboxylic acid dihydrazone) and DCDH = (2,6- pyridine diacarbonyl di chloride- N-N'-Pyridine-2,6-dicarboxylic acid dihydrazone) and (BF_4)=Tetrafluoroborate. The ligand and complexes have been analyzed for elemental analysis, spectral studies, and conductivity measurements. Different techniques like FT-IR, electronic data were used to investigate the structural features of the synthesized compounds. Electronic absorption and IR spectra indicate octahedral geometry. The antimicrobial activity of ligand and hydrazone derivatives and their vanadium complexes against bacteria and fungi shows the complexes have been found to be manifold active biologically than the ligand.

Key Words: Hydrazone derivatives, FT-IR, Spectral and antimicrobial Studies.

INTRODUCTION:

Hydrazones is a class of organic compounds having the basic structure $R_1R_2C=NNH_2$. They are important intermediates in heterocyclic chemistry. Hydrazone moiety plays an important key role in heterocyclic chemistry.[1-7] The most important property of hydrazones is their high physiological activity.[8-13] Extensive studies have revealed that the lone pair on trigonally hybridized nitrogen atom of the azomethine group is responsible[14-18] for the chemical and biological activity. It has been reported that metal complexes of hydrazones have diverse applications. Many researchers have synthesized these compounds as well as their metal complexes as plasticizers, polymerization inhibitors and antioxidants. They are used as fungicides and pesticides in biological and biochemical context.

EXPERIMENTAL:

Materials &Methods

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

Synthesis of Ligand

1:2 stoichiometric quantities of Pyridine 2, 6 Dicarboxalic acid ester (1.43 gm., 0.01M) and hydrazine hydrate ($0.83cm^3$, 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 off-white crystal in bottom round flask was concentrated to one-third of its original volume. Then, the obtained solution was cooled overnight and off-white crystals were filtered, washed with alcohol and ether then dried in vacuum over anhydrous $CaCl_2$ in a desiccator.

Complexes Synthesized from Pyridine 2, 6 Dicarboxalic acid ligand

1:1:1stoichiometric quantities of pyridine 2,6 dicarboxalic acid dihydrazide (1.97 gm., 0.01M), vanadium acetate (1.85gm., 0.01M) and 2,6-diacetyl pyridine (1.63gm., 0.01M) were mixed in 25ml. ethanol with continuous stirring. The solution obtained was refluxed over a water-bath for around 6-7 hours. After, concentrating to one-third of its original volume. It was subjected to addition of a small quantity of Sodium tetrafluoroborate and solution was cooled overnight when pale-yellow crystals separated out. The crystals were filtered, washed with alcohol and ether and dried in vacuum over anhydrous $CaCl_2$ in a desiccator.

Complexes synthesized from pyridine 2, 6 dicarboxalic acid ligand

Equimolar quantities of pyridine 2,6 dicarboxalic acid dihydrazide (1.97 gm., 0.01M), vanadium acetate (1,85gm., 0.01M) and 2,6-pyridine dicarbonyldichloride (1.90 gm., 0.01M) were mixed in 25ml. ethanol with constant stirring. The solution obtained was refluxed over a water-bath for around 6-7 hours. Thereafter it was concentrated to one-third of its original volume. Then, a small amount of sodiumtetrafluoroborate was added and solution was cooled overnight when dark-yellow crystals separated out. The crystals were filtered, washed with alcohol and ether and 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)*. 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 4000-400 cm^{-1}. The electronic spectra of complexes in DMSO were recorded on a UV-VIS-NIR *(Cary5E)* spectrophotometer at room temperature.

Table-1 Elemental analysis and molar conductivity data of the ligand and newly synthesized

V(II) hydrazone Complexes

Compound	M.P.(°C)	Color	Molecular Weight [F/(c)]	Elemental Analysis (%) (F/C)				Molar Conductivity ($Ohm^{-1}cm^2mol^{-1}$)
				C	H	N	M	
PDA	142	Off-White	197.11 (197.19)	42.61 (42.64)	5.58 (5.62)	35.51 (35.52)	-	-
V(II)[DPDH]$(BF_4)_2$	263	Pale-Yellow	550.85 (550.90)	35.85 (34.88)	3.26 (3.29)	15.24 (15.26)	9.13 (9.25)	113.23
V(II)[DCDH]$(BF_4)_2$	244	Dark Yellow	591.70 (591.74)	28.39 (28.42)	2.04 (2.04)	14.29 (14.20)	9.53 (8.61)	113.18

INFRA-RED DATA:

The band due to the -NH_2 group disappeared completely in the complexes. The band due to the -NH group did not show any change in the spectra of complexes, confirming that the Nitrogen of -NH group did not take part in reaction whereas a sharp band was seen in the range of 1370 cm^{-1} proving that -NH_2 group is present in the ligand. Some entirely new absorption band appeared in the spectra of complexes viz. band around 560-550cm^{-1} due to M-N group, a band around 460-450cm^{-1} due to M-O group . These new band confirmed the coordination of nitrogen and oxygen with the metal atom in the complexes.

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

S. No.	Functional Groups	[PDA]	V(II)[DPDH]$(BF_4)_2$	V(II)[DCDH]$(BF_4)_2$
1.	-CH_2	2900	2870	2860
2.	-NH_2	1370	-	-
3.	-NH	3330	3320	3320
4.	N-N	950	940	930
5.	>C=N	-	1610	1600

6.	>C=O	1680	1630	1640
7.	M-N	-	560	550
8.	M-O	-	450	460

Figure-1 Infra-red spectrum of ligand PDA

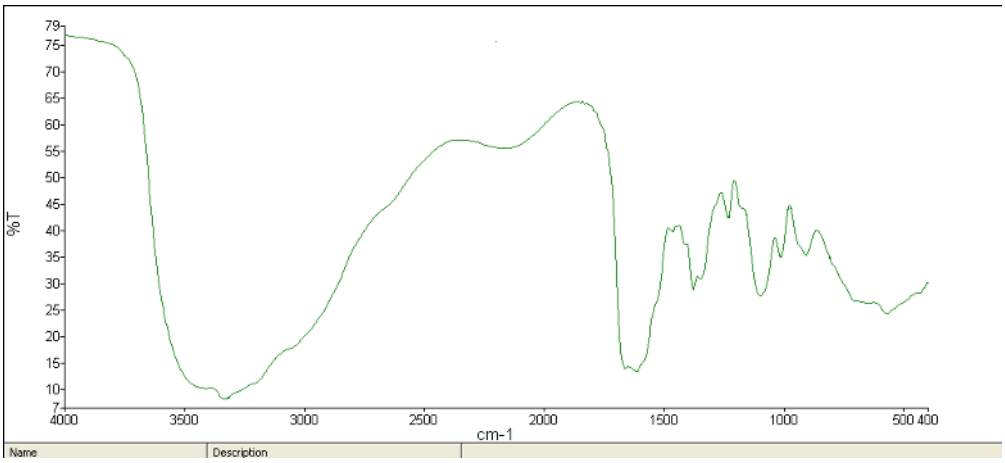


Figure- 2 Infra-red Spectrum of synthesized hydrazone complex V(II)[DPDH](BF$_4$)$_2$

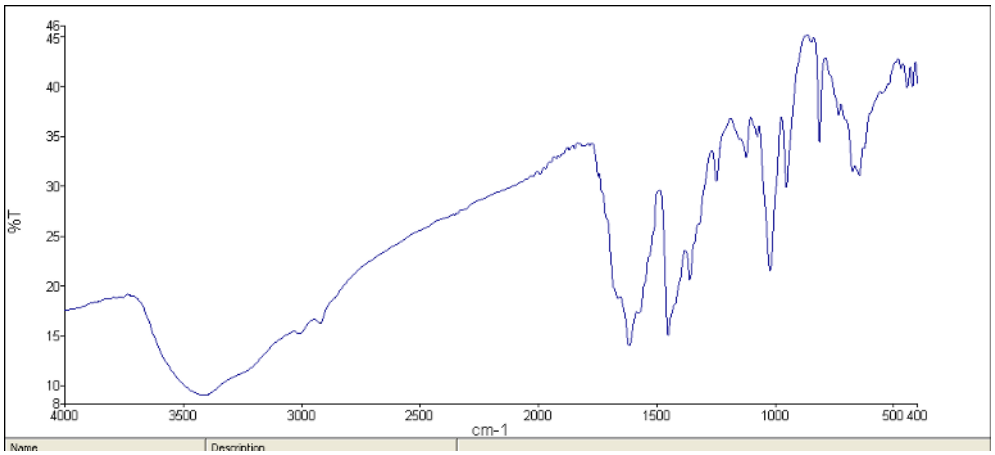
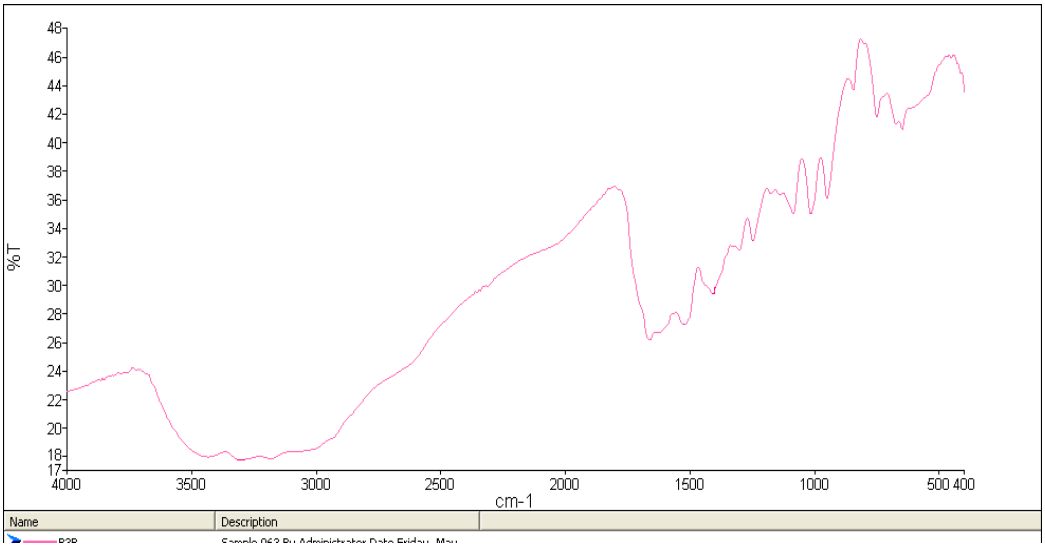


Figure- 3 Infra-red spectrum of synthesized hydrazone complex V(II)[DCDH](BF$_4$)$_2$



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 12,400-11,900 cm^{-1} attributed to $^2Eg \rightarrow {}^2T_2g$ transition and in the range of 24,500-24,150cm^{-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 synthesized complexes

S. No.	Complexes	Transition (cm^{-1})	
		$^2E_g \rightarrow {}^2T_{2g}$	L→M
1.	V(II)[DPDH]$(BF_4)_2$	11900	24150
2.	V(II)[DCDH]$(BF_4)_2$	12400	24500

ANTIMICROBIAL ACTIVITY:

Agar Well Diffusion Method

The antimicrobials present in the compound are allowed to diffuse out into the medium and interact in compound and sealed with test microorganism. The resulting zone of inhibition will be uniformly circular as there will be a confluent lawn of growth.

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 100µg/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 µg/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 µg/ml., 75 µg/ml., 50 µg/ml., 25 µg/ml., 12.5 µg/ml., 6.25 µg/ml., 3.125 µg/ml., 1.562 µg/ml., 0.78 µg/ml. and 0.39 µg/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)

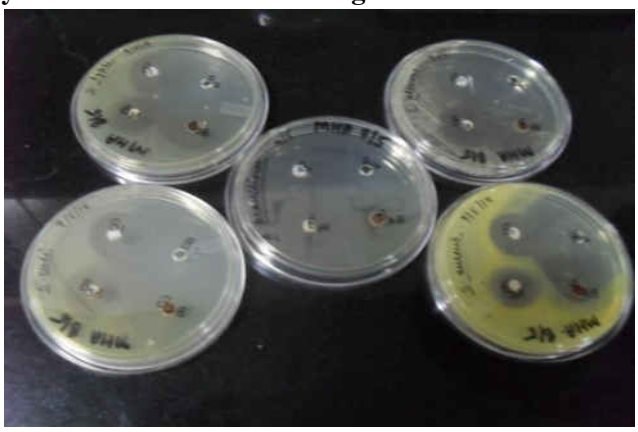
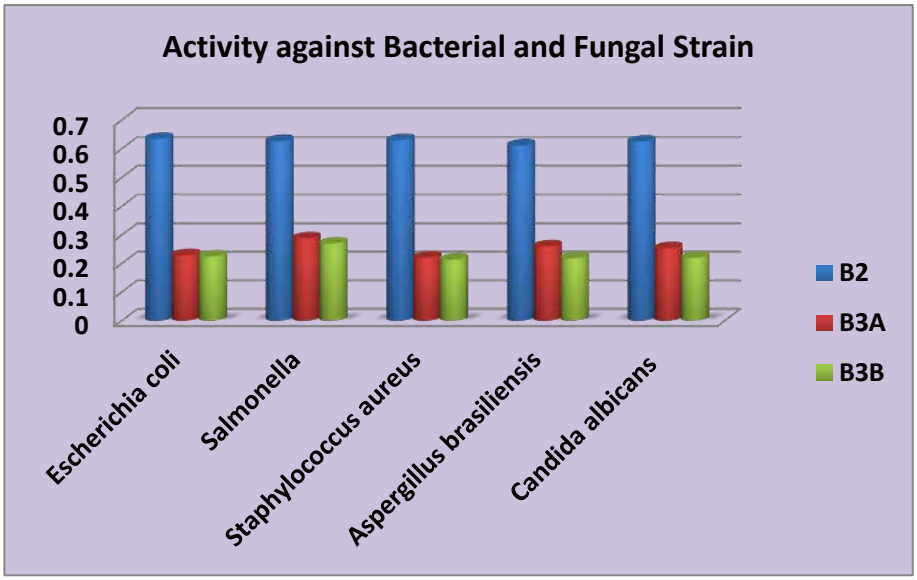


Table-4 Minimum Inhibitory Concentration (MIC) value in Molar Concentration [X10^{-4}] of Ligand and Newly Synthesized complexes

Compounds	Activity against bacterial strain			Activity against fungal strain	
	E. coli (Gram Negative)	***Salmonella*** (Gram Negative)	***S. aureus*** (Gram Positive)	***A. brasiliensis***	***C. albicans***
PDA	0.635	0.627	0.630	0.612	0.625
V(II)[DPDH](BF$_4$)$_2$	0.230	0.289	0.221	0.261	0.254
V(II)[DCDH](BF$_4$)$_2$	0.225	0.271	0.214	0.219	0.220

Figure-5 Activity against Bacterial and Fungal Strain



Abbreviation :

B2- PDA

B3A- V(II)[DPDH](BF$_4$)$_2$

B3B- V(II)[DCDH](BF$_4$)$_2$

CONCLUSION:

In the present paper, we have synthesized and characterized hydrazone derivatives and their vanadium complexes, formulated as V(II)[DPDH](BF$_4$)$_2$and V(II)[DCDH](BF$_4$)$_2$. Both the complexes are solid and colored. The complexes are stable at room temperature. The ligand and hydrazone derivatives and their vanadium complexes are off-white, pale-yellow and dark-yellow in color and are soluble in DMSO and DMF. All compounds give satisfactory elemental analyses results as shown in the Table-1. According to infra-red spectral graph and data in Figure -1,2,3 and Table-2, Nitrogen, Oxygen are suitably placed for coordination towards the metal ion which has been proposed for both complexes. It is absence in ligand and presence in both complexes confirms an octahedral geometry of complex I and complex II. On the basis of all analytical and spectral data both complexes were having octahedral geometry as evidences by the Electronic Spectral and Infra-Red spectral results. Electronic spectra data of ligand and hydrazone derivatives and their vanadium complexes shown in Table-3.The Minimum Inhibitory Concentration (MIC) value in molar concentration of ligand and hydrazone derivatives and their vanadium complexes shown in Figure-4,5 and in Table-4. The antimicrobial screening data confirms that the metal complexes exhibit a higher inhibitory effect than the free ligand.

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