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Der Pharma Chemica, 2010, 2(5):377-382
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X

Synthesis, characterization and biological evaluation of macrocyclic schiff bases with oxovanadium (V) complexes

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ABSTRACT

The macrocyclic ligands are synthesized by condensation of o-phenylene diamine and 4-4 diamino, diphenyl methane with acetyl acetone in ethanolic medium followed by formation of their complexes with pentavalent vanadium salt of type $VO(acac)_2$. Ligands and complexes have been characterized with the help of melting point, molecular weight, conductance, TLC determination, element analysis, magnetic moment and electronic, IR, ^{1}HNMR spectral analysis. On the basis of these studies, four coordinated square planar geometry for these complexes has been proposed. The biological activities of all compounds have been studied by screening them against organisms Gram negative E.coli, and Gram positive S.aureus, M.luteus and B.licheniformis(ATCC).

Keywords: Macrocyclic ligands, Vanadium complexes, Antibacterial Activities.

INTRODUCTION

Macrocyclic Schiff bases are very important molecules in biological systems. They have wide range of applications in bioinorganic, coordination & catalysis field [1, 2]. They have some interesting properties and biological functions such as being models for metalloproteins & oxygen carrier systems, in catalyzing organic oxidation ion reaction. These ligands found to be very versatile due to their capability of forming stable complexes[3,4].

On the other hand vanadium found to be very important element as it exhibit variety of insulin mimetic properties [5]. Vanadium possesses medicinal, pharmacological & biological application also in many enzymatic reactions. Research interest in V/O chemistry derives from its utility in several biological and industrial processes. The coordination chemistry of vanadium has acquired renewed interest since the discovery of vanadium in organisms such as certain

ascidians and Amanita mushrooms and as a constituent of the cofactors in vanadate-dependent haloperoxidases and vanadium nitroginase [6, 7]. Keeping the above facts in mind and in continuation of our research work on vanadium (V) complexes with macrocyclic Schiff bases, in the present paper we report the synthesis and characterization of vanadium (V) complexes with macrocyclic Schiff bases derived from the condensation of o-phenylene diamine and 4-4 diamino diphenyl methane with acetyl acetone.

MATERIALS AND METHODS

All the chemicals used in present investigation were of A.R. quality. O-phenylene diamine and 4, 4 diamino, diphenyl methane were of CDH, Acetylacetone was of Thomas Baker. All the solvents used were of high purity and distilled in the laboratory before use.

Purity of the compounds was judged by using silica gel TLC plates and spots were visualized by iodine vapours. Melting points were taken in open capillaries using Sunsim electric melting point apparatus and are uncorrected. Molecular weights were determined by Rast Camphor method. The conductivity values of 10^{-3} M solution in DMF measured on Equiptronics model no. EQ-660A. Magnetic susceptibilities of the compounds were determined at room temperature by Guoy Balance using mercury tetraisocynato cobaltate as the calibrant.

IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in range 4000- 500cm^{-1} using KBr pellets and ^{1}HNMR spectra in MeOD at 300 MHz using TMS as an internal standard. The ligands and complexes were analysed for C, H &N. All done at CDRI, Lucknow.

The biological activities of the compounds carried out by paper disc diffusion method against various bacteria [8, 9]. The IC_{50} values for all compounds were also determined.

Synthesis of Macrocyclic Schiff base (PDAc)

An ethanolic solution of O-phenylene diamine(1mol ,0.540gm) and acetylacetone (1mol, 0.500ml) in equimolar ratio were mixed. The resulting mixture was refluxed for several hours in large amount of ethanol. The solid crystals were collected and dried over $CaCl_2$ in vaccum and were recrystallised by ethanol & Petroleum ether.

The colour of ligand was dark green. (65% yield, mp-100°C).

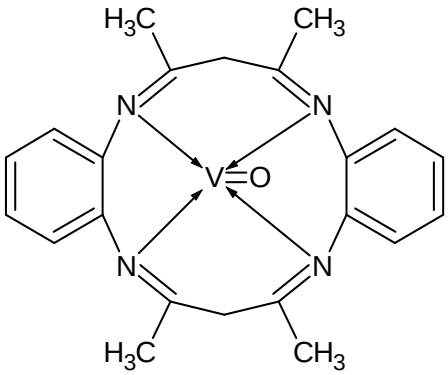

FIG 1: Proposed structure of oxovanadium complex with (PDAc)

Synthesis of Vanadium (V) complex with (PDAc)

The complex of Vanadium (v) has been prepared by reacting an ethanolic solution of vanadium acetylacetone salt with ethanolic solution of prepared (PDAc) ligand in 1:1 molar ratio. Resulting reaction mixture was refluxed on water bath for 5-6 hours.

Brownish black powder was obtained & recrystallised by petroleum ether (60-80°C). (70% yield, mp-135°C.)

Synthesis of Macrocyclic Schiff base (DDMAc)

An ethanolic solution of 4,4-diamino,diphenyl methane(1mol,0.99gm) and acetylacetone (1mol, 0.500ml) in equimolar ratio were mixed with constant stirring. The resulting mixture was refluxed for several hours in large amount of ethanol. The solid crystals were collected and dried over $CaCl_2$ in vaccum and were recrystallised by ethanol & Petroleum ether. (60-80°C).
The color of ligand was light brown. (65% yield, mp-125°C).

Synthesis of Vanadium (V) complex with (DDMAc)

The complex of Vanadium (v) has been prepared by reacting an ethanolic solution of vanadium acetylacetone salt with ethanolic solution of prepared (DDMAc) ligand in 1:1 molar ratio. Resulting reaction mixture was refluxed on water bath for 5-6 hours.
Brownish black powder was obtained & recrystallised by petroleum ether (60-80°C). (70% yield, mp-155°C).

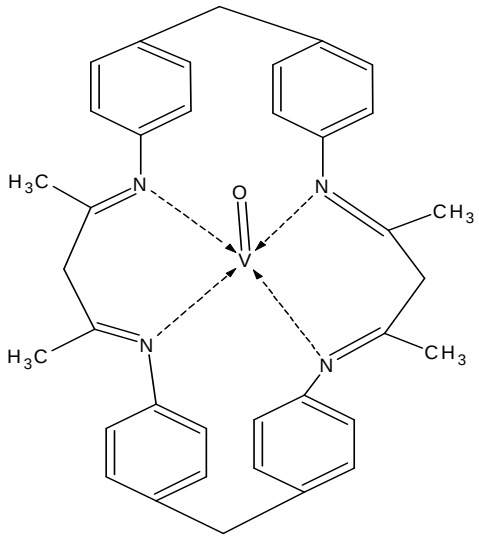

FIG 2: Proposed structure of oxovanadium complex with (DDMAc)

RESULTS AND DISCUSSION

The resulting macrocycic Schiff bases and their vanadium complexes are colored and soluble in methanol, ethanol, DMF& DMSO. They have sharp melting points and are stable at room temperature and are non-hygroscopic. Compounds are pure as both ligands and complexes moves as a single spot indicating the presence of only one component and hence their purity.

Molecular weights determined by Rast Camphor method and were found in accordance with calculated value. The monomeric nature of these ligands and complexes is confirmed by molecular weight determinations. The conductivity values of 10^{-3} M solution in DMF (ranges between 3- 30ohm^{-1} cm^{2} mol^{-1}), showing their non-electrolyte nature. The Oxovanadium complexes were found to be diamagnetic in nature. This may be explained on the basis of electronic configuration of central metal ion. The central metal ion V (V) does not possess any unpaired electron.

The microanalytical datas are given below:-

Table: - 1 Microanalytical datas of ligands and their Oxovanadium complexes

COMPOUND	YIELD IN %	COLOUR	MWF (C)	MP IN °C	ELEMENT ANALYSIS IN % FOUND (CALCD)				
					C	H	N	O	V
LIGAND (PDAc) $C_{22}H_{24}N_4$	65	DARK GREEN	(341) 344	100	75.14 (76.74)	7.01 (6.97	17.83 (16.27)	-	-
VANADIUM COMPLEX OF (PDAc) $C_{22}H_{24}N_4OV$	70	BROWNISH BLACK	(410) 412	135	62.95 (64.07)	6.01 (5.82)	14.18 (13.59)	3.01 (3.88)	12.62 (12.64)
LIGAND (DDMAc) $C_{36}H_{36}N_4$	65	LIGHT BROWN	(522) 524	125	81.56 (82.44)	7.82 (6.87)	10.42 (10.68)	–	–
VANADIUM COMPLEX OF(DDMAc) $C_{36}H_{36}N_4OV$	70	BROWNISH BLACK	(590) 592	155	71.68 (72.97)	7.19 (6.08)	9.21 (9.45)	2.89 (2.70)	9.01 (8.78)

Electronic spectra of ligand (PDAc) shows weak band at 260nm and 300nm attributable to π- π* and n-π* transition respectively, in its complex first remains unchanged while second shows blue shift and a band appear at 250nm due to donation of N lone pair of C=N group to vanadium atom. Ligand (DMAc) shows the same weak band at 245nm and 340nm while second appears at 300nm.

The IR spectra of ligands shows strong band in the region1590-1640cm-1 due to C=N which is assignable to macrocyclic Schiff bases. In spectra of vanadium complexes , very sharp peak in region 970-990cm^{-1} suggests the presence of V=O bond.. The band due to C=N has shifted to lower frequency in the complexes indicating the coordination through azomethine nitrogen.

The ^{1}HNMR spectra of ligand (DDMAc) shows signal between δ7.20-7.37 due to aromatic ring which gets shifted downfield and appears between δ7.23-7.44 in its oxovanadium complex. The proton signal for methylene group appears between δ3.69-3.83 also shifted downfield and appears between δ3.90-3.98. In case of (PDAc) spectra between δ7.16-7.46 gets shifted to δ7.18-8.00 due to aromatic ring.

Biological Activities

The plates of Muller Hinton agar medium were uniformly seeded with the bacterium to be tested like Gram negative *E.coli,*and Gram positive *S.aureus, M.luteus* and *B.licheniformis* (ATCC)

Small sterile discs of whatman no.1 filter paper, impregnated with standard solution of test compounds were placed on the plates of culture medium at different concentration of 100,500 and 1000ppm. Plates were immediately transferred to incubator. After one day of incubation, the degree of sensitivity is determined by measuring the zone of inhibition. In all determinations tests were performed in triplicate and the results were taken as a mean of three determinations[10-12]. Ofloxacin was taken as the standard. All the ligands and their oxovanadium complexes have shown significant inhibition comparable to standard. Results are shown as mean ±SEM in table 2, also the IC_{50} values are shown in table 3.

Table: - 2 Biological results of ligands and their complexes showing zone of inhibition (in mm) analyzed as Mean±SEM

Bacteria	Conc In ppm	Ligand PDAc (Mean±SEM)	Complex of PDAc (Mean±SEM)	Ligand DDMAc (Mean±SEM)	Complex of DDMAc (Mean±SEM)
E. coli(-ive)	100	14±0.355	17±0.204	15±0.462	17±0.360
	500	23±0.346	26±0.289	23±0.152	27±0.462
	1000	28±0.204	31±0.346	29±0.173	32±0.355
S.aureus(+ive)	100	15±0.289	18±0.462	16±0.404	18±0.404
	500	23±0.231	27±0.231	25±0.355	28±0.231
	1000	29±0.251	32±0.115	29±0.346	32±0.173
M.luteus(+ive)	100	16± 0.115	18±0.360	14±0.289	18±0.360
	500	24± 0.462	27±0.173	23±0.251	27±0.289
	1000	28±0.404	31±0.355	28±0.115	32±0.115
B.licheniforms(+ ive)	100	15±0.173	17±0.404	15±0.418	18±0.251
	500	23±0.289	26±0.204	24±0.418	27±0.204
	1000	29±0.360	32±0.462	29±0.231	32±0.346

Significance level P< 0.00, (n=3)

Table: - 3 Showing the IC_{50} values (in mg/ml) against various bacteria

Compound	IC_{50} values (in mg/ml) against			
	E. coli(-ive)	S.aureus(+ive)	*M.luteus* (+ive)	*B.licheniforms*(+ ive)
Ligand PDAc	0.50	0.50	0.44	0.50
Complex of PDAc	0.31	0.23	0.23	0.31
Ligand DDMAc	0.50	0.39	0.50	0.50
Complex of DDMAc	0.28	0.21	0.23	0.23

CONCLUSION

Thus on the basis of all structural evidences the tentative structure with possibly four coordinated oxovanadium(V) complexes can be proposed with having square planar geometry of both oxovanadium complexes of ligands (PDAc) and (DDMAc).
The results of biological activities showed that Vanadium complexes are more bacterial active then their precursor macrocyclic ligands due to chelation and also the zone of inhibition increases with the concentration.

Acknowledgement
The authors are thankful to Head , Dept. of chemistry , Government college Ajmer for providing the research facilities and to CDRI , Lucknow for providing all spectral and elemental analysis and also to MDSU, Ajmer for providing us all the bacteria.

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