Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2015, 7(12):205-209
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Oxovanadium(IV) complexes with tetraaza macrocyclic ligands derived by condensation of 1,2-diacetylbenzene with o-phenylenediamine

Vijai Singh, Probin Bora and Hardeo Singh Yadav*

Department of Chemistry, North Eastern Regional Institute of Science and Technology, Nirjuli, Itanagar, Arunachal Pradesh, India

---

ABSTRACT

The synthesis oxovanadium(IV) complex, $[VO(L)]SO_4$, is achieved using in-situ method, where VO^{2+} ion acts as a kinetic template for the formation of ligand derived by condensation of 1,2-diacetylbenzene with o-phenylenediamine in 1:2 molar ratio in aqueous ethanol medium. The parent complex, $[VO(L)]SO_4$, after reaction with β-diketones, result macrocyclic complexes, $[VO(mac)]SO_4$, where mac = macrocyclic ligands derived by reactions of $[VO(L)]SO_4$ with acetylacetone, benzoylacetone, thenoyltrifluoroacetone and dibenzoylmethane.These vanadyl complexes are characterized and their tentative structures are ascertained on the basis of elemental analyses, molar conductance, magnetic moments and spectral (electronic, infra-red and esr) data. All the vanadyl complexes are five-coordinate having tetradentate chelating ligands.These vanadyl complexes were tested for their antifungal activities against Aspergillus niger and Aspergillus flavus, which showed significant antifungal activities.

INTRODUCTION

The coordination chemistry of transition metals with Schiff base ligands have resulted many interesting molecules focused to model for metal - containing sites in metallo-proteins and enzymes [1-5]. In recent years, Schiff base complexes of VO^{2+} has attracted huge interest involving ligands with nitrogen and oxygen donor atoms [6]. Role of vanadium in enzymatic systems such as in the haloperoxidases [7-9], phosphorylation [10], insuline mimicking [11-12], prophylaxis against carcinogenesis [13]. These findings have induced curiosity resulting more emphasis to study vanadium role in biological systems. There are reports that vanadium enters into the organism by inhalation, the gastrointestinal tract and the skin, which is specifically stored in certain organs mainly in the liver, Kidney and bones. In order to explore the pharmaceutical applications of vanadyl ion in complexed form, a series of oxovanadium(IV) complexes with ligands derived by condensation of 1,2-diacetylbenzene with o-phenylenediamine in 1:2 molar ratio in aqueous ethanol medium and their cyclization with β-diketones is reported, where vanadyl ion play a key role as kinetic template. The antifungal studies of these vanadyl complexes are carried out against Aspergillus niger and Aspergillus flavus.

MATERIALS AND METHODS

Materials

Reagent grade chemicals and solvents were used in the synthesis. Vanadyl sulphate, 1,2-Diacetylbenzene and o-phenylenediamine used were Aldrich products. The β-diketones such as acetylacetone, benzoylacetone, thenoyltrifluoroacetone and dibenzoylmethane were Sisco Research Laboratory products.

Analytical and Physical Measurements

Standard gravimetric method was used for quantitative estimation of Vanadium as its sodium vanadate [14]. Estimation of Sulphur was made as barium sulphate [15]. The standard method for determination of melting point (uncorrected) was employed using sulphuric acid bath. Toshniwal conductivity bridge, model no. CLO102A was used for conductance measurements at room temperature. The magnetic susceptibility of the complexes in powder form was carried out at room temperature using Guoy's balance. Mercury tetrathiocyanatocobaltate(II), $Hg[Co(CNS)_4]$, (X_g = 1644 x 10^{-6} c.g.s. unit at 20^0 C) was used as calibrant. The electronic spectra of the complexes were recorded on Beckmann DU-2 spectrophotometer in the ranges 2000 – 185 nm using dimethylformamide as solvent. The room temperature and liquid nitrogen temperature e.s.r. spectra were recorded at SAIF, IIT Mumbai, India. The infrared spectra of the complexes were measured on IRAffinity-1, FTIR spectrophotometer, SHIMADZU using KBr pellets in the range 4000 cm^{-1} – 200 cm^{-1}.

Antifungal studies

The oxovanadium(IV) complexes were tested for their antifungal activity against the fungi Aspergillus flavus and Aspergillus niger using standard methods [16]. Fluconazole (75 µg/mL) was used as a standard drug. The stock solutions of the oxovanadium(IV) complexes (100 µg/mL) were prepared in dimethylformamide (DMF) and were added to potato dextrose sugar (PDA). This mixture was poured into sterile Petri dishes and allowed to solidify. Fungal spores were inoculated at the centre of the medium. Finally, the Petri dishes were incubated at 303 K for 72 hours. The percentage inhibition was calculated by the equation :

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

Where C is the diameter of the fungal colony in control plate and T is diameter of fungal colony test plate.

In-situ synthesis of oxovanadium(IV) complex with ligand derived by condensation of 1,2-diacetylbenzene with o-phenylenediamine (1:2)

Vanadyl sulphate (2 mmol) was dissolved in methanol (25 mL), which was added into a refluxing solution of 1,2-diacetylbenzene (2 mmol) and o-phenylenediamine (4 mmol) in ethanol (25 mL). The reflux of reaction mixture was continued for 5 hours, when the color of the solution turned green with little precipitation. A dark green color product was isolated after evaporating solvent under vacuum. The isolated complex was thoroughly washed with methanol / ethanol (1:1) mixture (10 mL).

$[VO(L)]SO_4$

Yield (78%); D.P. > 268^0 ; IR(ν_{max}, KBr, cm^{-1}): 1610(>C=N) , 304(V-N), 980 (V=O), 1135, 956, 600 (SO_4^{2-}), 3352 (assy.), 3170(sym.) (N-H); UV (ν, cm^{-1}): 11130 ($^2B_2 \rightarrow {}^2E$) , 15200 ($^2B_2 \rightarrow {}^2B_1$), 21300 ($^2B_2 \rightarrow {}^2A_1$), 35200 (>C=N) ; Anal. Cacl. for $C_{22}H_{22}N_4O_5SV$ (504.94) (%): C- 52.28, H- 4.36, N-11.09, S- 6.34, V- 10.08; Found (%): C- 52.60, H- 4.40, N- 11.12, S- 6.38, V- 10.06.

In-situ synthesis of macrocyclic complexes of oxovanadium(IV) using β-diketones as cyclizing reagents

Vanadyl sulphate (2 mmol) was dissolved in methanol (25 mL), which was added into a refluxing solution of 1,2-diacetylbenzene (2 mmol) and o-phenylenediamine (4 mmol) in ethanol (25 mL). The reflux of reaction mixture was continued for 5 hours, when the color of the solution turned green with little precipitation. To this reaction mixture, an ethanolic solution (10 mL) of acetylacetone (2 mmol) and glacial acetic acid (1 mL) were added. This reaction mixture was reflued further for about 3 hours which resulted green precipitate after cooling it under refrigerator. The vanadyl complex was purified by washing with the methanol / ethanol (1:1) mixture (10 mL). The similar procedure was followed for the synthesis of other oxovanadium(IV) macrocyclic complexes using benzoylacetone, thenoyltrifluoroacetone and dibenzoylmethane.

$[VO(mac^1)]SO_4$

Yield (68%); D.P. > 278^0 ; IR(ν_{max}, KBr, cm^{-1}): 1615(>C=N) , 305(V-N), 982 (V=O), 1134, 955, 605 (SO_4^{2-}) ; UV (ν, cm^{-1}): 11230 ($^2B_2 \rightarrow {}^2E$) , 15250 ($^2B_2 \rightarrow {}^2B_1$), 21350 ($^2B_2 \rightarrow {}^2A_1$), 35300 (>C=N) ; Anal. Cacl. for $C_{27}H_{26}N_4O_5SV$ (504.94) (%): C- 56.95, H- 4.57, N-9.84, S- 5.63, V- 8.95; Found (%): C- 52.60, H- 4.40, N- 11.12, S- 6.38, V- 10.06.

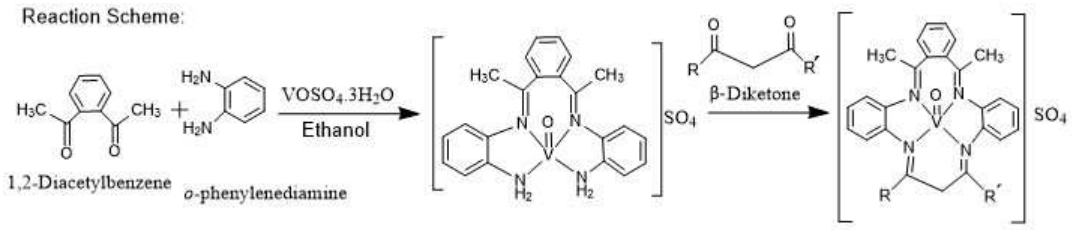
[VO(mac^2)]SO_4
Yield (65%); D.P. > 288^0 ; IR(ν_{max}, KBr, cm^{-1}): 1612(>C=N) , 306(V-N), 980 (V=O), 1136, 958, 608 (SO_4^{2-}) ; UV (ν, cm^{-1}): 11330 ($^2B_2 \rightarrow {}^2E$) , 15300 ($^2B_2 \rightarrow {}^2B_1$), 21380 ($^2B_2 \rightarrow {}^2A_1$), 35350 (>C=N) ; Anal. Cacl. for $C_{32}H_{28}N_4O_5SV$ (630.94) (%): C- 60.86, H- 4.44, N-8.88, S- 5.07, V- 8.07; Found (%): C- 60.98, H- 4.48, N- 11.32, S- 6.08, V- 8.08.

[VO(mac^3)]SO_4
Yield (66%); D.P. > 284^0 ; IR(ν_{max}, KBr, cm^{-1}): 1612(>C=N) , 305(V-N), 984 (V=O), 1134, 960, 606 (SO_4^{2-}) ; UV (ν, cm^{-1}): 11340 ($^2B_2 \rightarrow {}^2E$) , 15350 ($^2B_2 \rightarrow {}^2B_1$), 21370 ($^2B_2 \rightarrow {}^2A_1$), 35340 (>C=N) ; Anal. Cacl. for $C_{30}H_{23}N_4O_5S_2F_3V$ (690.94) (%): C- 52.10, H- 3.33, N-8.10, S- 9.26, V- 7.37; Found (%): C- 52.22, H- 3.36., N- 8.12, S- 9.08, V- 7.40.

[VO(mac^4)]SO_4
Yield (64%); D.P. > 280^0 ; IR(ν_{max}, KBr, cm^{-1}): 1610(>C=N) , 306(V-N), 980 (V=O), 1138, 956, 605 (SO_4^{2-}) ; UV (ν, cm^{-1}): 11300 ($^2B_2 \rightarrow {}^2E$) , 15370 ($^2B_2 \rightarrow {}^2B_1$), 21390 ($^2B_2 \rightarrow {}^2A_1$), 35390 (>C=N) ; Anal. Cacl. for $C_{37}H_{30}N_4O_5SV$ (692.94) (%): C- 64.07, H- 4.33, N-8.08, S- 4.61, V- 7.35; Found (%): C- 64.00, H- 4.30, N- 8.00, S- 4.61, V- 7.32.

RESULTS AND DISCUSSION

The reaction scheme for the formation of vanadyl complexes are presented below:



Where,

R	R´	β-Diketone
$-CH_3$	$-CH_3$	Acetylcetone
$-C_6H_5$	$-CH_3$	Benzoylacetone
$-C_4H_3S$	$-CF_3$	Thenoyltrifluroacetone
$-C_6H_5$	$-C_6H_5$	Dibenzoylmethane

As shown in the reaction scheme, the parent oxovanadium(IV) complex was synthesized by in-situ method by refluxing the reaction mixture containing vanadyl sulphate, 1,2-diacetylbenzene and o-phenylenediamine in 1:1:2 molar ratios in aqueous ethanol medium. The reaction appear to proceed as follows:

$VOSO_4.3H_2O$ + 1,2-Diacetylbenzene + o-Phenylenediamine $\rightarrow$ $[VO(L)]SO_4$ + 5 H_2O

The oxovanadium(IV) complex was reacted with β-diketones in 1:1 molar ratio, which resulted formation of macrocyclic complexes, $[VO(mac)]SO_4$, by condensation of terminal amino group with ketonic group of β-diketones. The elemental analyses of the oxovanadium(IV) complexes show 1:1 metal to ligand stoichiometry.

INFRARED SPECTRA
The complex, $[VO(L)]SO_4$, show bands at 1610 cm^{-1}, which may be assigned to the coordinated azomethine group [16]. The bands appearing at 3352 cm^{-1} and 3170 cm^{-1} may be assigned to asymmetrical and symmetrical N-H stretching modes of the non-coordinated terminal amino groups of the ligand, L [17]. A band at 304 cm^{-1} further support the coordination of nitrogen atom to vanadium, which may be assigned to v (V-N) vibrations [18]. The presence of an intense band at 980 cm^{-1} may be assigned to v (V=O) vibration [19]. The ionic sulfate group in the complex is indicated [20] by three bands at 1135 cm^{-1} (ν_3), 956 cm^{-1} (ν_1) and 600 cm^{-1} (ν_4). The absence of ν_2

band and non-splitting of v_3 band indicate that Td symmetry is retained. The infrared bands of macrocyclic oxovanadium(IV) complexes have similar patterns except that $v_{asym.}$ and $v_{sym.}$ vibrations of terminal -NH_2 group disappear in cyclisation reaction with β-diketones.

MAGNETIC MOMENT AND ELECTRONIC SPECTRA

The magnetic moment values of all the oxovanadium(IV) complexes were found in the range 1.71 - 1.73 B.M. at room temperature, which are well within the range reported for vanadyl complexes with paramagnetic centre [21]. This data confirm mononuclear nature of oxovanadium(IV) complexes. The electronic spectra show bands in the regions 11,130 cm^{-1} - 11,340 cm^{-1}, 15,200 cm^{-1} - 15370 cm^{-1} and 21300 cm^{-1} - 21390 cm^{-1} which are in accordance to other reports for oxovanadium(IV) complexes involving nitrogen / oxygen donor atoms. According to Ballhausen and Gray scheme, these electronic bands have been assigned to $^2B_2 \rightarrow {}^2E$, $^2B_2 \rightarrow {}^2B_1$ and $^2B_2 \rightarrow {}^2A_1$ transitions respectively. One more electronic band observed in the region 35,200 - 35,390 cm^{-1} may be assigned to the transition arising out of azomethine linkages [22].

ESR SPECTRA

The X-band esr spectra of the oxovanadium(IV) complexes were recorded at room temperature and liquid nitrogen temperature, which show eight lines due to hyperfine splitting originating basically from the interaction of unpaired electron with a ^{51}V nucleus having the nuclear spin no. I = 7/2 [23-25]. Anisotropy is not visible at room temperature because of rapid tumbling of molecules in solution and only g-average values are obtained. However, anisotropy is clearly visible in the spectra at liquid nitrogen temperature and eight lines each due to $g_{\parallel}$ and $g_{\perp}$ are observed separately showing $g_{\parallel} < g_{\perp}$ and $A_{\parallel} > A_{\perp}$. The $g_{\parallel}$, $g_{\perp}$, $A_{\parallel}$ and $A_{\perp}$ values, which are measured from the esr spectra, are in good agreement for square pyramidal structure.

Table.3 X-Band ESR spectral data of oxovanadium(IV) complexes

Complex	Room Temp.	Liquid nitrogen temperature					
	$\langle g \rangle$	$g_{\parallel}$	$g_{\perp}$	$\langle g \rangle$	$A_{\parallel}$	$A_{\perp}$.	$\langle A \rangle$
$[VO(L)]SO_4$	1.980	1.930	1.970	1.956	190.70	66.48	107.88
$[VO(mac^1)]SO_4$	1.982	1.932	1.973	1.959	190.80	65.90	107.53
$[VO(mac^2)]SO_4$	1.981	1.931	1.972	1.958	190.60	65.88	107.45
$[VO(mac^3)]SO_4$	1.982	1.932	1.973	1.959	190.72	65.90	107.50
$[VO(mac^4)]SO_4$	1.982	1.931	1.972	1.958	190.71	65.92	107.51

Antifungal Activity

The oxovanadium(IV) complexes were tested for their antifungal activity against the fungi Aspergillus flavus and Aspergillus niger and significant antifungal activity but $[VO(mac^3)]SO_4$ was found to exhibit most active , which may be due to sulphur and fluorine atoms present in the thenoyltrifluoroacetone, a cyclising agent as β-diketone. The percentage inhibition was calculated by the equation :

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

Where C is the diameter of the fungal colony in control plate and T is diameter of fungal colony in test plate. The antifungal activity of the oxovanadium(IV) complexes are summarized below:

Complex	Zone of inhibition (in %)*		Conc. (µg/mL)
	Aspergillus flavus	Aspergillus niger	
$[VO(L)]SO_4$	64	68	100
$[VO(mac^1)]SO_4$	63	69	100
$[VO(mac^2)]SO_4$	66	68	100
$[VO(mac^3)]SO_4$	76	80	100
$[VO(mac^4)]SO_4$	67	69	100
**Fluconazole	100	100	75

***Standard Drug , * average of three replicates*

The antifungal activity of oxovanadium(IV) complexes is attributed due to reduced polarity of metal ion after coordination by ligand molecule, which could enhance the lipophilic character of the central metal ion facilitating it to be more permeable through the lipid layer of cell membrane. It significantly enhance the antifungal property of VO(IV) complexes.

Acknowledgment
One of the author Vijai Singh is thankful to the Director, NERIST, Nirjuli-791109, Itanagar Arunachal Pradesh, India for extending all facilities to complete this research work.

REFERENCES

[1] M.Shebl, *Spectrochim. Acta A: Mol. Biomol. Spectrosc*., **2008**, 70, 850-859.
[2] P. Przybylski, A Huczynski, K. Pyta, B. Brzezinski, F. Bartl, *Curr. Org. Chem.*, **2009**, 13, 124-148.
[3] A. A.Khandar, S. A. Hosseini-Yazdi, S. A. Zarei, *Inorg. Chim. Acta*., **2005**, 358, 3211-3217.
[4] P. K. Mascharak, *Coord. Chem. Rev*., **2002**, 225, 201-214.
[5] V. E. Kaasjager, L. Puglisi, E. Bouwman, W. L. Driessen, J. Reedijk, *Inorg. Chim. Acta*., **2000**, 310, 183-190.
[6] R. C. Mourya, S. Rajput, *J. Mole. Struct*., **2006**, 794 (1-3), 24-34.
[7] A. Butler, J. V. Walker, *Chem. Rev*., **1993**, 93, 1937-1944.
[8] A. Andersson, A. Willetts. S.Allenmark, *J. Org. Chem.*,**1997**, 62, 8455-8458.
[9] H. B. ten Brink, H. E. Schoemaker, R. Wever, *Eur. J. Biochem*., **2001**, 268, 132-138.
[10] C. R. Cornman, E. P. Zovinka, M. H. Meixner, *Inorg. Chem*.,**1995**, 34, 5099-5100.
[11] Y. Shechter, I. Goldwaser, M. Mironchik, M. Fridkin, D. Gefel, *Coord. Chem. Rev*., **2003**, 237, 3-11.
[12] A. M. B. Bastos, J. G. da Silva, P. I. S. Maia, *Polyhedron*, **2008**, 27, 1787-1794.
[13] P. Noblia, M. Vieites, B. S. Parajon-costa, *J. Inorg. Biochem*., **2005**, 99, 443-451.
[14] A. I. Vogel; A Text Book of Quantitative Inorganic Analysis, 4th ed., Longmans Green Co.Ltd., London, **1978**.
[15] A. I. Vogel; A Text Book of Practical Organic Chemistry, 4th ed., Longmans Green Co. Ltd., London, **1978**.
[16] C Yuan, L. Lu, X. Gao, M. Guo, Y. Li, X. Fu, M. Zhu, *J. Biol. Inorg. Chem*., **2009**, 14, 841-85.
[17] P. B. Sreeja, M. R. P. Kurup, *Spectro chimica Acta Part* A, **2005**, 61 331-336.
[18] M. Nonoyama, S. Tomita, K. Yamasaki, *Inorganica Chimica Acta*, **1975**, 12, 33-37.
[19] K. Sakata, M. Kuroda, S. Yanagida, M. Hashimoto, *Inorganica Chimica Acta*, **1989**, 156, 107-112.
[20] S. Samanta, D. Ghosh, S. Mukhopadhyay, A. Endo, T.J.R. Weakley, M. Chaudhury, *Inorg. Chem*., **2003**, 42, 1508.
[21] M. Tsuchimoto, G. Hoshina, N. Yoshioka, H. Inoue, K. Nakajima, M. Kamishima, M. Kojima, S. Ohba, J. *Solid State Chem.*, **2000**, 153, 9.
[22] A. Sarkara, S. Pal, *Inorg. Chim. Acta*, **2008**, 361, 2296.
[23] A. Christos, Dimitra J. Kontogiorgi, Hadjipavlou-Litina, *Bioorg. Med. Chem. Lett*., **2004**, 14,611.
[24] A. P. Mishra, L. R. Pandey, *Indian J. Chem*. A, **2005**, 44 A, 94.
[25] R. Tan, C. Li, Z. Peng, D. Yin, D., D. Yin, *Catalysis Commun*., **2011**, 12, 1488.
[26] R. Ando, M. Nagai, T. Yagyu, Masunobu, *Inorg. Chim. Acta*, **2003**, 351, 107.