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In-situ Synthesis of Oxovanadium(IV) complexes with ligands derived by condensation of Benzil with Amino acids

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Abstract

The in-situ method of synthesis has been used to isolate oxovanadium(IV) complexes with ligands derived by reaction of benzil with amino acids such as glycine, alanine, serine, cysteine and valine, where template effect of VO^{+2} cation appears to play an important role. The complexes are characterised by elemental analysis, magnetic moment measurements and spectral (infrared, electronic and electron spin resonance) data. The oxovanadium (IV) complexes are five coordinate, having tetradentate ligand derived from benzil being precursor molecule. The antifungal activities of isolated vanadyl complexes are tested against the fungi *Aspergillus flavus* and *Candida glaberata.*

Keywords: Oxovanadium(IV); benzyl; aminoacid; template effect

1. Introduction

Vanadium has attracted attention as a biologically relevant metal found in both anionic and cationic forms having oxidation states from -1 to +5 in its compounds[1-3]. The physiological action of oxovanadium(IV) complexes have been found to show insulin mimetic activity [4-5] and potent anti-diabetic agents [6]. However, the poor absorption of vanadium compounds into the blood from the gastrointestinal tract [7] require higher doses of vanadium to reach therapeutically useful levels, but efficacious doses often reach toxic level [8]. When vanadium is coordinated with organic ligands, it results in higher uptake of vanadium in tissues and higher mobility of compounds which helps to reduce the required vanadium dosage [9-10]. In order to explore the pharmaceutical importance of vanadyl ion in biological systems, a series of oxovanadium(IV) complexes with ligands derived by reaction of benzil with amino acids such as glycine, alanine, serine, cysteine and valine were synthesised where VO^{+2} cation appears to act as template.

2. Experimental

2.1. Materials and Methods

All the chemicals and solvent used were Analytical grade Reagent and were used without further purification. Oxovanadium(IV) complexes were prepared by standard method using hydrated salt of vanadyl sulphate.

2.2. Analytical methods and physical measurements

The analysis of carbon, hydrogen and nitrogen was carried out at Sophisticated Analytical Instrument Facility, Indian Institute of Technology, Bombay by using CHN analyser (Model: FLASH EA 1112 series). Infrared spectra of the complexes were recorded in KBr medium on a Perkin-Elmer Paragon 1000 Fourier-transform spectrometer and collected data were plotted in X-Y axis using Spectrum software. ESR spectra were recorded at liquid nitrogen temperature by using Electron Spin Resonance Spectrometer, VARIAN, USA, Model: E-112 ESR Spectrometer, Specification: X- band microwave frequency 9.5 GHz.

2.3. In-situ preparation of oxovanadium (IV) complexes with ligands derived by condensation of benzil with glycine

Oxovanadium(IV) sulphate (2 mmol) dissolved in ethanol (25 mL) was added to refluxing solution of benzil (2 mmol) and glycine (4 mmol) in ethanol (25 mL). The mixture was refluxed for 3 hours when the colour of the solution turned green. The solvent was removed under *vacuo* at room temperature and the dark green colour compound

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was isolated. The complex were thoroughly washed with ethanol. Yield 65 %.

A similar procedure was adopted to obtain oxovanadium (IV) complexes with ligand derived by condensation of benzil with alanine, serine, cysteine and valine.

The physical and analytical data of the complexes

Complex I: E. F. $VC_{18}H_{14}N_2O_5$, m.p. 545K, Anal data Calcd: C,55.55; H, 3.60; N,5.30;O, 20.57; V, 13.09 %. Found: C,55.58; H, 3.59; N, 7.31; V, 13.07 %

Complex II: E. F. $VC_{20}H_{18}N_2O_5$, m.p.553K, Anal data Calcd: C, 57.56; H, 4.32; N, 6.72; O, 19.19; V, 12.22 %. Found: C, 57.55, H, 4.30; N, 6.74; V, 12.24 %

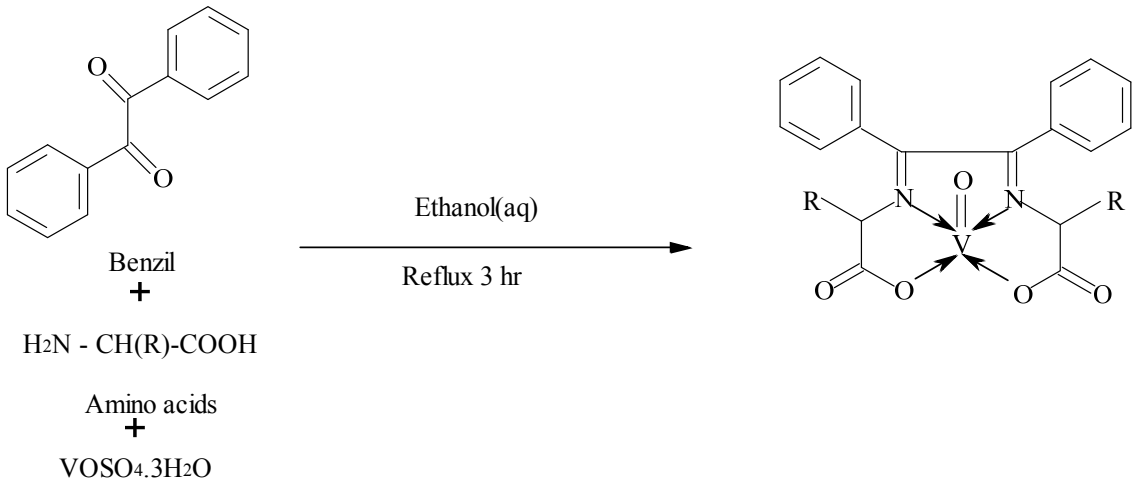
Complex III: E. F. $VC_{20}H_{18}N_2O_5$, m.p.554K, Anal data Calcd: C,53.46, H,4.00; N, 6.24; O,24.95; V,11.35 %. Found: C, 53.48; H, 3.99; N,6.22; V,11.37 %

Complex IV: E.F.$VC_{20}H_{18}N_2O_5S_2$, m.p.558K, Anal data Calcd: C,49.99; H,3.74, N,5.82; O,16.63; S,13.31,V,10.59%.Found: C,50.00; H,3.78; N,5.85; S, 13.34; V,10.60%

Complex V: E. F. $VC_{24}H_{26}N_2O_5$, m.p.553K; Anal data calcd:C, 60.22; H,5.59; N,6.02; O, 17.21; V, 10.95%. Found:C,60.23; H,5.60; N.6.04;V,10.98 %

3. Results and Discussion

The oxovanadium (IV) complexes were synthesized using in-situ method by refluxing the reaction mixture of benzil, amino acid and vanadyl sulphate in 1 : 2 : 1 molar ratio in aqueous ethanol. The reaction appears to proceed according to the scheme shown in Fig. 1. The elemental analysis of complexes show 1: 1 metal to ligand stoichiometry.



[Where, R: -H, $-CH_3$, $-CH_2OH$, $-CH_2SH$, and $-CH(CH_3)_2$]

Fig. 1. Reaction scheme for the synthesis of oxovanadium(IV) complexes

3.1. Infrared Spectra

The oxovanadium (IV) complexes show >C=N absorption at about 1620–1616 cm^{-1} which is normally observed at 1660 cm^{-1} in free ligands [11-13]. The lowering of this band in the oxovanadium (IV) complexes support coordination N-atoms of azomethine groups to the vanadyl ion [11-14]. It is further supported by a band at 305 cm^{-1}, which may be assigned to ν (V-N) vibration [15]. The presence of ν(>C=N) band and the absence of ν(>C=O) band at about 1700 cm^{-1} support the coordination of–NH_2 group of amino acids with the keto group of benzil.

The ν_{asym}(O–C–O) and ν_{sym}(O–C–O) stretching vibration of carboxylic group(–COOH) in free amino acids are observed at ca. 1530 cm^{-1} and 1415 cm^{-1} respectively, giving Δ(O–C–O) value of the order of 115 cm^{-1}. The respective ν_{asym}(O–C–O) and ν_{sym}(O–C–O) in case of oxovanadium(IV) complexes occurs at ca. 1560 cm^{-1} and 1425 cm^{-1}, giving Δ(O–C–O) value at 135 cm^{-1}, which is higher than the free amino acids. Such increase in the Δ(O–C–O) values support [16] the monodentate coordination of the amino acids through carboxyl group. Thus, these observations indicate that the monovalent anionic species of the amino acids are coordinated to the vanadium centre. Oxovanadium(IV) show an intense band at around 980–985 cm^{-1}, which is assigned to the ν(V=O) vibration [17].

3. 2. Magnetic moment and Electronic Spectra

The room temperature magnetic moment values for the oxovanadium(IV) complexes are in the range 1.70–1.76 B.M. These values are in agreement with the reported values of oxovanadium(IV) complexes with solitary unpaired electron [18].

The electronic spectra show bands in the region 11450–11800 cm^{-1}, 15100–15850 cm^{-1} and 21200–2250 cm^{-1} similar to the other five coordinated oxovanadium(IV) complexes with tetradentate ligands. Such spectrum is explained considering $^2B_2 \rightarrow {}^2E$, $^2B_2 \rightarrow {}^2B_1$ and $^2B_2 \rightarrow {}^2A_1$ transitions as represented in literature [19]. One more band is observed in the region 35200–35700 cm^{-1}, which may be due to the transition involving azomethine linkage.

3. 3. ESR Spectra

The X- band electron spin resonance spectra of the oxovanadium(IV) complexes recorded in DMSO at room temperature and at liquid nitrogen temperature show eight lines which are due to hyperfine splitting arising from the interaction of the unpaired electron with a ^{51}V nucleus having the nuclear spin number I=7/2. The anisotropy is not noticed due to the rapid motion of molecules in solution at room temperature and g- average values were worked out. Anisotropy is clearly visible at liquid nitrogen temperature spectra and eight bands due to $g_{\parallel}$ and $g_{\perp}$ are observed. The $g_{\parallel}$, $g_{\perp}$, $A_{\parallel}$, $A_{\perp}$ values are measured from the spectra which are in good agreement for a square pyramidal structure [20-22].

Room temperature g values and liquid nitrogen temperature(LNT) g and A values of the oxovanadium(IV) complexes:

Complex I: Room temperature: $|g|$=1.972. Liquid nitrogen temperature: $g_{||}$=1.931, $g_{\perp}$=1.970, $|g|$=1.957, $A_{||}$=190.68, $A_{\perp}$=66.68, $|A|$=108.01

Complex II: Room temperature: $|g|$=1.980. Liquid nitrogen temperature: $g_{||}$=1.933, $g_{\perp}$=1.973, $|g|$=1.959, $A_{||}$=190.66, $A_{\perp}$=65.81, $|A|$=107.42

Complex III: Room temperature: $|g|$=1.981. Liquid nitrogen temperature $g_{||}$=1.932, $g_{\perp}$=1.972, $|g|$=1.958, $A_{||}$=190.89, $A_{\perp}$=65.75, $|A|$=107.45

Complex V: Room temperature: $|g|$=1.980. Liquid nitrogen temperature $g_{||}$=1.935, $g_{\perp}$=1.974, $|g|$=1.961, $A_{||}$=190.87, $A_{\perp}$=65.79, $|A|$=107.48

On the basis of the above analytical and spectral data, the tentative structures of the complexes are represented in Fig 1.

3. 4. Antifungal Activity

The synthesized oxovanadium(IV) complexes were tested against the fungi *Aspergillus flavus* and *Candida glaberata* by the standard method [23]. It was observed that the complex **IV** has more antifungal activity than other complexes **I**, **II**, **III** and **V** which may be due to the sulphur atom of cysteine.

The Amphotericin B(75 µg/mL) and Micoanazole (75µg/mL) were used as standard drugs.The stock solutions(100µg/mL) were prepared by dissolving the complexes in dimethyl sulphoxide(DMSO) and were added to potato dextrose agar (PDA). The mixture was poured into sterile Petri dishes and left to solidify. Fungus spores were suspended on the medium at the centre and finally the dishes were incubated at 301K for 72 hours. The percentage inhibition was calculated by the following equation:

$$\% \text{ inhibition} = \frac{(C - T)x100}{C}$$

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

Antifungal Activity (%inhibition) of oxovanadium(IV) complexes :

Complex I: Aspergillus flavus(54%), Candida glaberata(54%).

Complex II: Aspergillus flavus(56%), Candida glaberata-58%.

Complex III: Aspergillus flavus(60%), Candida glaberata-58%.

Complex IV: Aspergillus flavus(72%), Candida glaberata(70%).

Complex V: Aspergillus flavus(52%), Candida glaberata(54%).

Standard drugs: Amphotericin B -Aspergillus flavous(100%), Miconazole-Candida glaberata-(100%).

4. Conclusion

The spectral data show that the Schiff base condensation of benzil, a versatile molecule with amino acids is achieved by virtue of kinetic template effect of oxovanadium(IV) cation in aqueous ethanol medium. The tetradentate ligands are bonded with vanadyl ion through the azomethine nitrogen atoms and o-donor atoms of carboxylate group of the amino acids. On the basis of the analytical results, infrared, electronic, electron spin resonance spectral data and magnetic moment values, it is proposed that all the oxovanadium (IV) complexes are square pyramidal wherein presence of oxovanadium(IV) centre is also supported by esr studies. These oxovanadium(IV) complexes have shown potential antifungal activity.

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