



## Template Synthesis, Spectroscopic Characterization and Antimicrobial Studies of Oxovanadium(IV) Tetraazamacrocyclic Complexes Derived from 1, 8-Diaminonaphthalene and Substituted $\beta$ -Diketones

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**Abstract:** A new series of oxovanadium (IV) tetraazamacrocyclic complexes of type  $[\text{VO}(\text{mac})]\text{SO}_4$ , have been synthesized via *in situ* reaction of 1,8-diaminonaphthalene and substituted  $\beta$ -diketones (1-phenyl-3-(phenyl/4-chlorophenyl/4-hydroxyphenyl/4-methoxyphenyl/4-nitrophenyl)-diketone) in the presence of oxovanadium(IV) sulphate in methanol. Attempts to synthesize the corresponding metal free macrocyclic ligands did not prove successful. Complexes were characterized on the basis of elemental analyses, conductance measurements, magnetic properties and spectral (electronic, IR, and EPR) data. The magnetic moments of the complexes lie in the range 1.70-1.78BM suitable for complexes with one unpaired electron and paramagnetic nature. The infrared spectra indicates that the ligands coordinate through four aza nitrogen atoms to vanadium(IV). The fluid solution EPR spectra show an eight-line pattern typical for a mononuclear  $\text{VO}(\text{IV})$  complexes. The spectral studies support a square pyramidal geometry for the oxovanadium(IV) complexes. The oxovanadium complexes were tested for their antibacterial activity against bacteria *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and antifungal activity against fungi *Aspergillus niger* and *Candida albicans*. The complexes show moderate to good activity as compared to standard antibiotic tetracycline and the antifungal drug fluconazole.

**Keywords:** Macroyclic Complexes, Oxovanadium (IV),B-Diketones, Antibacterial, Antifungal

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## I. INTRODUCTION

During the recent years macrocyclic chemistry has attracted much attention and has become a growing class of research<sup>1-3</sup>. The intense interest in synthetic macrocycles and their metal complexes depend on the fact that they mimic naturally occurring macrocyclic molecules in their structural and functional features and on their rich chemical behavior<sup>4,5</sup>. The formation of macrocyclic complexes depends on the size of the macrocycle, on the nature of its donor atoms and on the complexing behavior of the anions involved in coordination<sup>4</sup>. The design and synthesis of complexes with aza macrocyclic ligands has remained a focus of scientific attention for many decades<sup>4</sup> and have attracted increasing interest in recent years for the possible relevance of these compounds as models, ligands for metal enzymes and metal proteins as metal ion selective ligands<sup>5</sup>. Condensation reactions between dicarbonyl and primary diamines have played an important role in the development of synthetic macrocyclic ligands<sup>5</sup>. *In situ* one pot template condensation reactions have been widely used for synthesis of such type of macrocyclic complexes, where the transition metal ions has been used as templating agent<sup>4,6</sup>. The metal ions direct the steric course of the reactions preferentially towards cyclic rather than oligomeric or polymeric products<sup>7</sup>. There is continued interest in synthesizing macrocyclic complexes because of their potential applications in the fundamental and applied sciences<sup>8,9</sup>. Transition metal macrocyclic complexes have received a great attention because of their biological activities, including antibacterial and antifungal<sup>10-12</sup>, antiviral, anticarcinogenic<sup>13</sup> and antifertile<sup>14</sup>. The chemistry of synthetic macrocyclic complexes are also of great importance due to their use as dyes and pigments<sup>15</sup>. Macroyclic metal chelating agents (DOTA) are useful for detecting tumor lesions<sup>16</sup>. Macroyclic complexes also find use in DNA binding and cleavage studies<sup>17</sup>. In order to explore the importance of vanadium(IV) azamacrocyclic complexes, a new series of oxovanadium(IV) complexes with macrocyclic ligands derived by the condensation of 1,8-diaminonaphthalene with substituted  $\beta$ -diketones (1-phenyl-3-(phenyl/4-chlorophenyl/4-hydroxyphenyl/4-methoxyphenyl/4-nitrophenyl)-diketone) were synthesized where  $\text{VO}^{2+}$  cation appears to act as template. The complexes were characterized with the help of various physicochemical techniques viz, elemental analyses, magnetic moment, conductance measurements and spectral (electronic, IR, EPR) data. To explore their antimicrobial activities, these macrocyclic complexes were also screened for their *in vitro* antibacterial activities against some bacterial strains viz., Gram negative *Escherichia coli* and Gram positive *Bacillus subtilis*, *Staphylococcus aureus*. The results obtained were compared with standard antibiotic tetracycline. The antifungal tests were done with fungal strain *Aspergillus niger*, and *Candida albicans*. The results obtained were compared with standard antifungal drug fluconazole.

## 2. MATERIALS AND METHODS

All the solvents and chemicals used were of reagent grade and used without further purification. Oxovanadium (IV) sulphate was procured from Aldrich Chemical Co. England. The  $\beta$ -diketones (1-phenyl-3-(phenyl/4-chlorophenyl/4-hydroxyphenyl/4-methoxyphenyl/4-nitrophenyl)-diketone) were synthesized by the condensation of acetophenone and different aromatic acid esters by reported method<sup>18</sup>.

### I.1 Preparation and isolation of complexes

All the oxovanadium (IV) azamacrocyclic complexes were synthesized by the template method. To a solution of oxovanadium (IV) sulphate (0.01 mol) in methanol (30 cm<sup>3</sup>), 1,8-diaminonaphthalene (0.02 mol) dissolved in methanol (30 cm<sup>3</sup>), and  $\beta$ -diketone (0.02 mol) in methanol (30 cm<sup>3</sup>) were added dropwise with stirring. The mixture was refluxed for ca. 11-18 h when dark brown coloured precipitate was obtained. The product was filtered off, washed with hot methanol and dried in vacuo. The purity of all the complexes was checked by thin layer chromatography. The product was identified to be a macrocyclic complex  $[\text{VO}(\text{mac})\text{SO}_4]$ . The complexes are stable in air and are soluble in dimethyl formamide, dimethyl sulphoxide and Nitrobenzene. The yield are about 65-70%.

### I.2 Analytical and Physical Measurements

Elemental analyses (C,H,N) were measured with a Perkin-Elmer 1400C analyzer. The vanadium metal was gravimetrically estimated as vanadate. Infrared spectra (4000–200 cm<sup>-1</sup>) of complexes were recorded as KBr pellets on a Jasco V650 Spectrophotometer. The magnetic susceptibility at room temperature was measured by Gouy's method. Electronic spectra of the complexes were recorded on Shimadzu UV-2600 UV-Visible-spectrophotometer using DMSO as a solvent. Conductance measurements were recorded in DMSO (10<sup>-3</sup>M) using Elico conductivity bridge type CM-82, provided with a dip type conductivity cell fitted with Pt electrodes. EPR spectra of complexes were recorded at room temperature and liquid nitrogen temperature using JEOL Model JES FA200 Electron Spin Resonance spectrometer.

### I.3 Antimicrobial Screening

Two bacteria *Escherichia coli* (MTCC 40) and *Bacillus subtilis* (MTCC 441 and one fungi *Aspergillus niger*, (MTCC 10180) were purchased from Microbial Type Culture Collection and Gene Bank (MTCC) CSIR-Institute of Microbial Technology, Sector-39A Chandigarh, India whereas One bacteria *Staphylococcus aureus* (MTCC 6571), and one fungi *Candida albicans* (MTCC 183) were collected from Department of Microbiology, BRD Medical college, Gorakhpur. The MIC (minimal inhibitory concentration) was obtained for drug as well as for compounds. The MIC is currently the standard test run for antibiotic sensitivity testing because it produces more pertinent information on minimal dosages.

### I.4 Antibacterial Screening

#### I.4.1 Agar dilution method

MIC (minimum inhibitory concentration) of compounds was calculated by the Agar dilution method. Minimum inhibitory concentrations (MICs) are defined as the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation, and minimum bactericidal concentrations (MBCs) as the lowest concentration of antimicrobial that will prevent the growth of an organism after subculture on to antibiotic-free media<sup>19</sup>. All the synthesized compounds were screened for their antimicrobial<sup>20,21</sup> activity (MIC) against various bacterial

strains *vz. Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus*. The dilution method<sup>22</sup> was applied for the determination of minimum inhibitory concentrations (MICs). The nutrient agar medium (28 gm) was mixed with 1000 mL of double distilled water and then autoclaved into an 80 mm sterile Petri plate. The corresponding bacterial broth or peptone solution was then added to the test sample DMSO solution (2.0mg/mL, 1.0 mg/mL, 0.5 mg/mL, 0.25 mg/mL, and 0.125 mg/mL). As a conventional drug, tetracycline was used. In triplicate plates, each bacterial strain was prepared and incubated at 37°C for 24h . As a minimum inhibitory concentration, the minimum concentration at which the compound showed inhibition at serial dilution of the concentration of compounds was recorded.

### 1.5 Antifungal screening

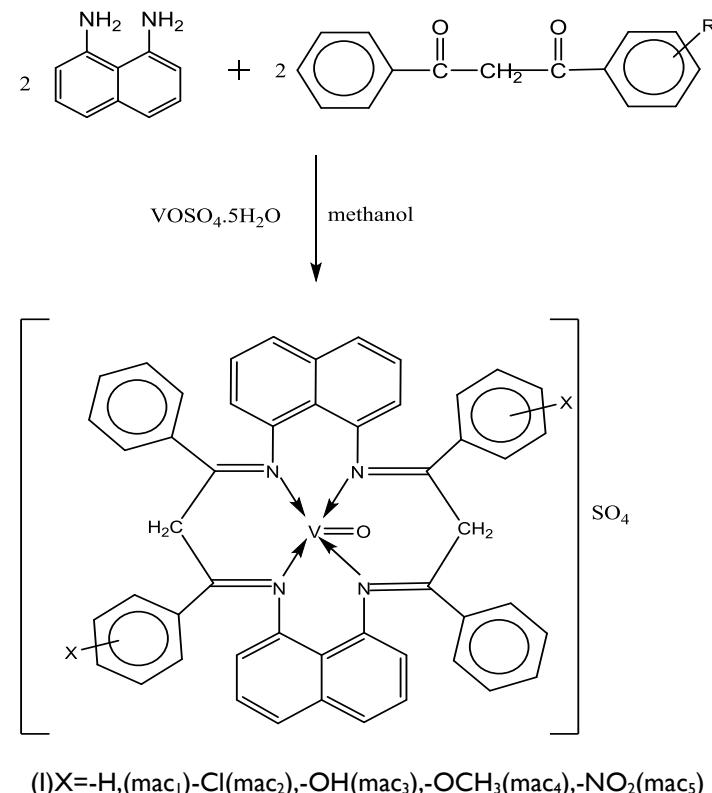
#### 1.5.1 Agar dilution method

All the synthesized compounds were screened for their antifungal activity against various fungi *Aspergillus niger* and *Candida albicans*. The agar dilution method<sup>22</sup> was applied for the determination of MIC by using standard guidelines. The sabouraud dextrose agar (SDA) medium (28 gm) was mixed

with 1000 mL of double distilled water and then autoclaved into an 80 mm sterile Petri plate. The corresponding fungal broth or peptone solution was then added to the test sample DMSO solution (2.0 mg/mL, 1.0 mg/mL, 0.5 mg/mL, 0.25 mg/mL, and 0.125 mg/mL). As a conventional drug, Fluconazole was used for control. In triplicate plates, each fungal strain was prepared and incubated at 37°C for 48h. As a minimum inhibitory concentration, the minimum concentration at which the compound showed inhibition at serial dilution of the concentration of compounds was recorded.

### 3. RESULTS AND DISCUSSION

Tetraazamacrocyclic oxovanadium (IV) complexes have been prepared by the reactions of 1,8-diaminonaphthalene with different substituted  $\beta$ -diketones in 1:1 molar ratio, respectively, using oxovanadium (IV) as template agent. All the macrocyclic complexes are of stoichiometry  $[\text{VO}(\text{mac})\text{SO}_4]$  (I), where (mac) is the macrocyclic ligand derived from condensation of 1,8-diaminonaphthalene with substituted  $\beta$ -diketones, according to Scheme-I.



**Scheme-I. Synthetic route for tetraazamacrocyclic complexes of oxovanadium(IV).**

All the macrocyclic complexes are dark brown coloured solid .The molar conductance values of the complexes in dimethyl formamide lie in the range 72-80 $\Omega^{-1}\text{cm}^2\text{mol}$ , indicating 1:1 electrolytic nature. The presence of an ionic sulphate group outside the coordination sphere was confirmed by the appearance of white precipitate with  $\text{BaCl}_2$

solution. Various attempts of crystallization were done to obtain a single crystal suitable for X-ray crystallography but were unsuccessful. However the elemental data analyses agree with the proposed mononuclear framework. The details of the reactions and analytical data of the complexes are given in Table-I.

**Table-1: Physical properties and analytical data of oxovanadium(IV) complexes.**

| Complex   | Empirical formula | color      | yield(%) | conductance<br>( $\Omega^{-1} \text{cm}^2 \text{ mol}^{-1}$ ) | Analysis %found (calcd.) |                |                |                |
|---|-------------------|------------|----------|---|--------------------------|----------------|----------------|----------------|
|   |                   |            |          |   | C                        | H              | N              | V              |
| $[\text{VO}(\text{mac}_1)]\text{SO}_4$ ( $\text{VC}_{56}\text{H}_{44}\text{N}_4\text{O}_5\text{S}$ )            |                   | Dark brown | 67       | 72  | 71.12<br>(71.10)         | 4.89<br>(4.85) | 6.24<br>(6.12) | 5.69<br>(5.55) |
| $[\text{VO}(\text{mac}_2)]\text{SO}_4$ ( $\text{VC}_{56}\text{H}_{50}\text{N}_4\text{O}_5\text{Cl}_2\text{S}$ ) |                   | Dark brown | 68       | 75  | 66.46<br>(66.38)         | 4.90<br>(4.97) | 5.73<br>(5.52) | 5.03<br>(5.00) |
| $[\text{VO}(\text{mac}_3)]\text{SO}_4$ ( $\text{VC}_{56}\text{H}_{52}\text{N}_4\text{O}_7\text{S}$ )            |                   | Dark brown | 70       | 78  | 68.96<br>(68.90)         | 5.37<br>(5.35) | 5.84<br>(5.72) | 5.12<br>(5.20) |
| $[\text{VO}(\text{mac}_4)]\text{SO}_4$ ( $\text{VC}_{58}\text{H}_{56}\text{N}_4\text{O}_7\text{S}$ )            |                   | Dark brown | 65       | 74  | 69.48<br>(69.35)         | 5.82<br>(5.60) | 5.68<br>(5.56) | 5.09<br>(5.06) |
| $[\text{VO}(\text{mac}_5)]\text{SO}_4$ ( $\text{VC}_{56}\text{H}_{50}\text{N}_6\text{O}_9\text{S}$ )            |                   | Dark brown | 66       | 80  | 65.15<br>(65.03)         | 4.87<br>(4.85) | 8.23<br>(8.10) | 4.83<br>(4.90) |

Where,

$\text{mac}_1$  = Macroyclic ligand derived from 1,8-diaminonaphthalene and 1-phenyl-3-(phenyl)-diketone  
 $\text{mac}_2$  = Macroyclic ligand derived from 1,8-diaminonaphthalene and 1-phenyl-3-(4-chlorophenyl)-diketone  
 $\text{mac}_3$  = Macroyclic ligand derived from 1,8-diaminonaphthalene and 1-phenyl-3-(4-hydroxyphenyl)-diketone  
 $\text{mac}_4$  = Macroyclic ligand derived from 1,8-diaminonaphthalene and 1-phenyl-3-(4-methoxyphenyl)-diketone  
 $\text{mac}_5$  = Macroyclic ligand derived from 1,8-diaminonaphthalene and 1-phenyl-3-(4-nitrophenyl)-diketone

### 3.1 Magnetic Moments and Electronic Spectra

The room temperature magnetic moments of the oxovanadium (IV) complexes lie in the range 1.70 to 1.78 B.M., corresponding to one unpaired electron. These values are well within the range reported for monomeric oxovanadium (IV) complexes<sup>23</sup>. The interpretation of the electronic spectra of oxovanadium (IV) complexes is a subject of continuing investigation and discussion. Several schemes have been advanced to interpret the electronic spectra of oxovanadium (IV) complexes. However, the electronic spectra of the oxovanadium (IV) complexes having a square pyramidal or a distorted octahedral

structure are most often interpreted in terms of the energy level scheme proposed by Ballhausen and Gray<sup>24</sup>. Such complexes usually show three bands viz.,  $^2\text{B}_2 \rightarrow ^2\text{E}$  ( $\nu_1$ ),  $^2\text{B}_2 \rightarrow ^2\text{B}_1$  ( $\nu_2$ ) and  $^2\text{B}_2 \rightarrow ^2\text{A}_1$  ( $\nu_3$ ). The  $\nu_3$  band is often obscured by intense charge-transfer absorptions. The spectra of the synthesized macrocyclic complexes exhibit two bands at ca. 12,500–13,200  $\text{cm}^{-1}$  ( $\nu_1$ ) and 19,000–19,500  $\text{cm}^{-1}$  ( $\nu_2$ ) and at one at ca. 30,000–30,500  $\text{cm}^{-1}$  probably due to an oxo  $\rightarrow$  vanadium(IV) charge-transfer admixed with  $^2\text{B}_2$  ( $d_{xy}$ )  $\rightarrow$   $^2\text{A}_1$  ( $d_z^2$ ) ( $\nu_3$ ) transition. These transitions fall in the same range as reported for other five coordinated ( $\text{C}_{4v}$ ) oxovanadium (IV) complexes.

**Table-2: Magnetic moments and electronic spectral bands of oxovanadium(IV) complexes**

| Complex                                | $\mu_{\text{eff}}(300 \text{ K})$<br>B.M. | Electronic spectral band ( $\text{cm}^{-1}$ ) |   |   |
|--|---|---|---|---|
|  |   | $^2\text{B}_2 \rightarrow ^2\text{E}$         | $^2\text{B}_2 \rightarrow ^2\text{B}_1$ | $^2\text{B}_2 \rightarrow ^2\text{A}_1$<br>+charge transfer |
| $[\text{VO}(\text{mac}_1)]\text{SO}_4$ | 1.78                                      | 13200   | 19500                                   | 30000   |
| $[\text{VO}(\text{mac}_2)]\text{SO}_4$ | 1.75                                      | 12800   | 19300                                   | 30100   |
| $[\text{VO}(\text{mac}_3)]\text{SO}_4$ | 1.70                                      | 12500   | 19000                                   | 30500   |
| $[\text{VO}(\text{mac}_4)]\text{SO}_4$ | 1.74                                      | 13000   | 19500                                   | 30300   |
| $[\text{VO}(\text{mac}_5)]\text{SO}_4$ | 1.75                                      | 12900   | 19200                                   | 30200   |

### 3.2 IR spectra

The infrared spectra of the complexes  $[\text{VO}(\text{mac})]\text{SO}_4$  do not show any band characteristics of the free carbonyl group (i.e. near 1670  $\text{cm}^{-1}$ ). Further a pair of bands at 3340 and 3380  $\text{cm}^{-1}$  corresponding to  $\nu$  ( $\text{NH}_2$ ) group present in the spectrum of 1,8-diaminonaphthalene are absent. The disappearance of these bands and appearance of a new band in the 1600–1625  $\text{cm}^{-1}$  region confirms the Schiff base condensation between  $\beta$ -diketone and 1,8-diaminonaphthalene<sup>11</sup>. The band is assigned to coordinated  $\nu$  ( $\text{C}=\text{N}$ ) stretching vibration. This also confirms the proposed macrocyclic ligand framework is formed<sup>11</sup>. The lower value of  $\nu$  ( $\text{C}=\text{N}$ ) may be explained on the basis of a drift of lone pair density of azomethine nitrogen towards the oxovanadium(IV) ion, indicating that coordination takes place through azomethine nitrogen<sup>22</sup>. This has been further corroborated by the appearance of a sharp band in the 400–

420  $\text{cm}^{-1}$  region, which may be assigned to ( $\text{V}-\text{N}$ )<sup>25</sup>. The spectra of all oxovanadium (IV) complexes show new bands at ca. 970–980  $\text{cm}^{-1}$  which are assigned to  $\nu$  ( $\text{V}=\text{O}$ ) vibration<sup>26</sup>. This frequency is in the range of the range 930–1040  $\text{cm}^{-1}$ , reported for a large set of oxovanadium complexes. The various absorption bands in the region 1400–1460, 1070–1100 and 720–760  $\text{cm}^{-1}$  may be assigned due to phenyl ring vibrations of the naphthalene ring<sup>11</sup>. The bands present in the region 1150–1170  $\text{cm}^{-1}$  in all complexes are assigned due to  $\nu$  ( $\text{C}-\text{N}$ ) stretching vibration<sup>11</sup>. The presence of an ionic sulphate group has been confirmed<sup>27</sup> by the appearance of three bands at ca. 1140 ( $\nu_3$ ), 920 ( $\nu_1$ ) and 610  $\text{cm}^{-1}$  ( $\nu_4$ ). The absence of a  $\nu_2$  band and non-splitting of  $\nu_3$  band indicate that  $\text{Td}$  symmetry is still held. Thus, the infrared spectral data indicates that the ligands act as  $\text{N}_4$  chelating agents and bonded with all four azomethine nitrogen atoms to the oxovanadium (IV).

**Table 3: Important infrared spectral bands of oxovanadium(IV) macrocyclic complexes ( $\text{cm}^{-1}$ ) and their assignments, where s = strong; m = medium; w = weak.**

| Complex                                | $\nu(\text{C}=\text{N})$ | $\nu(\text{C}-\text{N})$ | $\nu(\text{V}=\text{O})$ | $\nu(\text{V}-\text{N})$ | $\nu(\text{Phenyl ring})$ | $\nu(\text{SO}_4^{2-})$ |
|--|--------------------------|--------------------------|--------------------------|--------------------------|---------------------------|-------------------------|
| $[\text{VO}(\text{mac}_1)]\text{SO}_4$ | 1610s                    | 1150m                    | 970s                     | 410m                     | 1410m 1100 720w           | 1140m 910m 610w         |
| $[\text{VO}(\text{mac}_2)]\text{SO}_4$ | 1610s                    | 1170m                    | 972s                     | 412m                     | 1400m 1070 740w           | 1130m 900m 620w         |
| $[\text{VO}(\text{mac}_3)]\text{SO}_4$ | 1625s                    | 1160m                    | 980s                     | 410m                     | 1450m 1070 745w           | 1145m 915m 600w         |
| $[\text{VO}(\text{mac}_4)]\text{SO}_4$ | 1615s                    | 1155m                    | 972s                     | 415m                     | 1460m 1050 760w           | 1130m 910m 600w         |
| $[\text{VO}(\text{mac}_5)]\text{SO}_4$ | 1610s                    | 1165m                    | 975s                     | 455m                     | 1440m 1080 755w           | 1140m 920m 610w         |

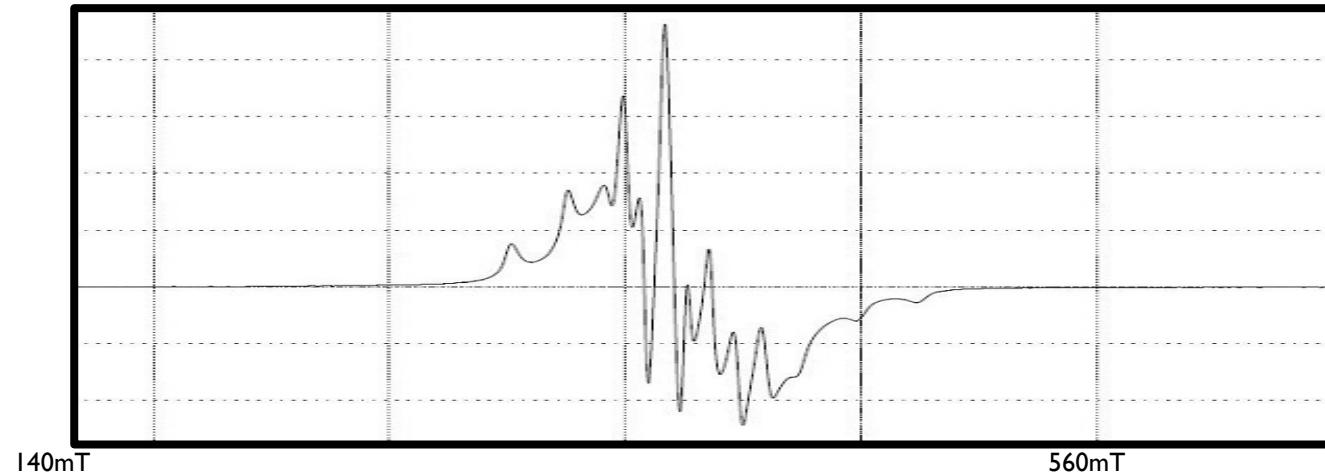
### 3.3 EPR Spectra

EPR spectroscopy provides information on the stereochemistry, ligand type and degree of covalency in the oxovanadium (IV) complexes. The EPR spectral parameters ( $g$  factor and hyperfine coupling constant  $A$ ) of the compounds reveal the model character of one compound. The X-band EPR spectra of oxovanadium(IV) macrocyclic complexes as shown in Figure 1 were recorded at room temperature and at liquid nitrogen temperature. These spectra in solution (DMSO) display typical eight-line patterns of vanadium ( $^{51}\text{V}$ ;  $I = 7/2$ ) with isotropic  $g_0$  values and hyperfine coupling parameters  $A_0$  (Table-3). The  $g$  average values determined from the spectra are  $\sim 1.98$ ,

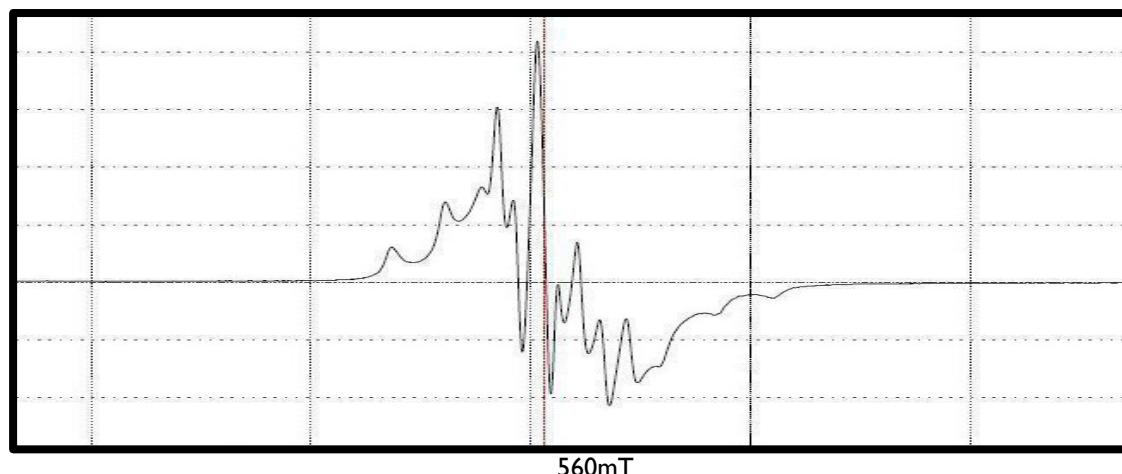
similar to the spin only value (free electron value) of 2.0023 suggesting little spin-orbital coupling. At the liquid nitrogen temperature, the spectra display well resolved axial anisotropy with two sets of eight-line patterns. The  $g_{\parallel}$ ,  $g_{\perp}$ ,  $A_{\parallel}$  and  $A_{\perp}$  values were evaluated and the values, thus obtained, are tabulated in Table-4. The values are typical of the spectra displayed by square pyramidal oxovanadium(IV) complexes<sup>28,29</sup> with unpaired electrons in an orbital of mostly  $d_{xy}$  character. The order of  $g_{\parallel} < g_{\perp}$  and  $A_{\parallel} >> A_{\perp}$  are consistent with oxovanadium(IV) sites in  $C_{4v}$  symmetry. All these complexes showed that  $g_{\parallel}$  values are less than 2.03 indicating that the present complex exhibits appreciable covalent nature.

**Table-4: EPR parameters of tetraazamacrocyclic oxovanadium(IV) complexes**

| Complexes                              | $g_{av}$ | $g_{\parallel}$ | $g_{\perp}$ | $A_{av}$ | $A_{\parallel}$ | $A_{\perp}$ |
|--|----------|-----------------|-------------|----------|-----------------|-------------|
| $[\text{VO}(\text{mac}_1)]\text{SO}_4$ | 1.982    | 1.966           | 1.990       | 87.7     | 133             | 65.0        |
| $[\text{VO}(\text{mac}_2)]\text{SO}_4$ | 1.980    | 1.946           | 1.997       | 91.0     | 139             | 67.0        |
| $[\text{VO}(\text{mac}_3)]\text{SO}_4$ | 1.984    | 1.956           | 1.998       | 86.2     | 132             | 63.4        |
| $[\text{VO}(\text{mac}_4)]\text{SO}_4$ | 1.983    | 1.957           | 1.996       | 90.1     | 141             | 64.6        |
| $[\text{VO}(\text{mac}_5)]\text{SO}_4$ | 1.988    | 1.968           | 1.998       | 88.6     | 136             | 64.9        |



**Fig 1: ESR spectra of  $[\text{VO}(\text{MDNB})\text{SO}_4]$  in DMSO at (a) Room Temperature**



(b) Liquid Nitrogen Temperature

### 3.4 Antibacterial Activity

All the chemically synthesized complexes were tested *in vitro* for their antibacterial activity as shown in Table 5. All the complexes of the tested series possess good to moderate antibacterial activities against all the bacterial strains. The MIC (minimum inhibitory concentration) shown by the complexes was compared with MIC obtained by standard antibiotic tetracycline (Table-5, Figure-2). The minimum inhibitory concentration is the lowest concentration of the antimicrobial agent that prevents the visible growth of the microorganisms after overnight incubation. The maximum activity (MIC=0.125 mg/mL) against *B. subtilis* and (MIC=0.25

mg/mL) for *E.coli* and *S.aureus* was shown by the complex  $[\text{VO}(\text{mac}_2)]\text{SO}_4$ . The good activity was also shown by the complex  $[\text{VO}(\text{mac}_5)]\text{SO}_4$  which showed (MIC=0.25mg/mL) for *S.aureus* and *B. subtilis* while (MIC=0.50mg/mL) for *E.coli*. These results suggest that electron withdrawing groups in the macrocyclic group play an important role in enhancing the activity. The significant inhibition was displayed by all oxovanadium (IV) complexes against all strains of Gram positive bacteria rather than Gram negative. The extra outer layer on the cell wall of the Gram negative bacteria acts as a barrier and needs high penetration of the compounds to reach the cells<sup>30</sup>.

Table5: Bacterial screening data of the oxovanadium (IV) complexes

| Complexes                              | Compound No. | Minimum inhibitory concentration (MICs) in mg/mL |                    |                  |
|--|--------------|--|--------------------|------------------|
|  |              | Gram negative                                    |                    | Gram Positive    |
|  |              | <i>E. coli</i>                                   | <i>B. subtilis</i> | <i>S. aureus</i> |
| $[\text{VO}(\text{mac}_1)]\text{SO}_4$ | C1           | 1.00   | 0.50               | 0.50             |
| $[\text{VO}(\text{mac}_2)]\text{SO}_4$ | C2           | 0.25   | 0.125              | 0.25             |
| $[\text{VO}(\text{mac}_3)]\text{SO}_4$ | C3           | 1.00   | 0.50               | 0.50             |
| $[\text{VO}(\text{mac}_4)]\text{SO}_4$ | C4           | 0.50   | 0.50               | 0.50             |
| $[\text{VO}(\text{mac}_5)]\text{SO}_4$ | C5           | 0.50   | 0.25               | 0.25             |
| Tetracycline                           |              | 0.125  | 0.125              | 0.125            |

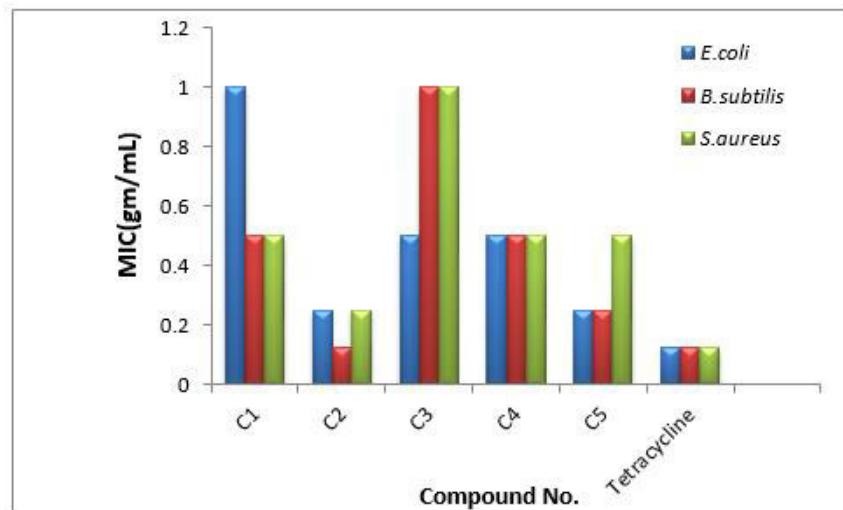


Fig 2: Comparison of MIC of complexes with standard antibiotic

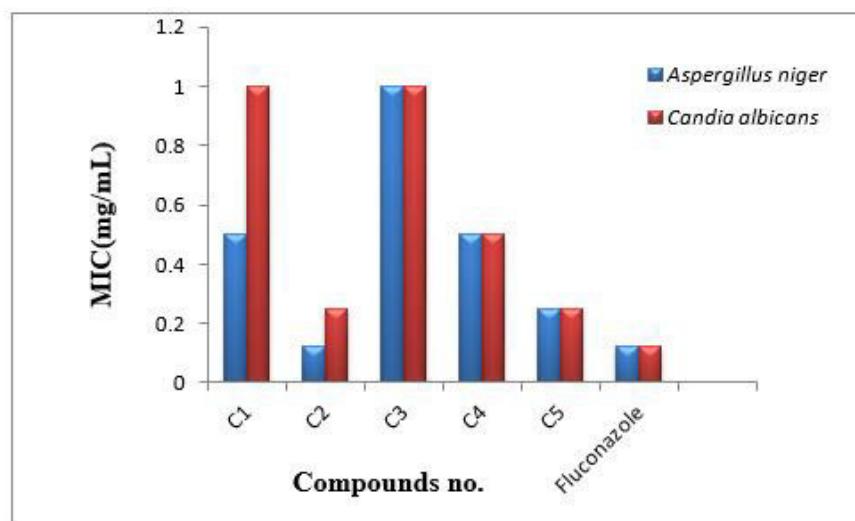
### 3.5 Antifungal Activity

The antifungal tests were done with fungal strain *Aspergillus niger* and *Candida albicans* for antifungal activity (Table-6, Fig.3). The results were compared with the standard antifungal drug fluconazole. Oxovanadium(IV) macrocyclic complexes containing -Cl group and -NO<sub>2</sub> group showed better activity than other complexes. C2 and C5 complexes

showed slightly higher activity against *A.niger* as compared to *C.albicans*. Though the complexes possess activity, it could hardly reach the effectiveness of the standard drug fluconazole. Some compounds C1 and C3 are less effective. This may be because the variation in effectiveness depends on either on the impermeability of the cells of the microbes or on difference in the ribosomes of the microbial cells<sup>30</sup>.

**Table6 : Fungicidal screening data of the tetraaza macrocyclic oxovanadium(IV) complexes**

| Compounds                              | Compound No. | Minimum inhibitory concentration (MICs) in mg/mL |                         |
|--|--------------|--|-------------------------|
|  |              | <i>Aspergillus niger</i>                         | <i>Candida albicans</i> |
| [VO(mac <sub>1</sub> )]SO <sub>4</sub> | C1           | 0.50   | 1.00                    |
| [VO(mac <sub>2</sub> )]SO <sub>4</sub> | C2           | 0.125  | 0.25                    |
| [VO(mac <sub>3</sub> )]SO <sub>4</sub> | C3           | 1.00   | 1.00                    |
| [VO(mac <sub>4</sub> )]SO <sub>4</sub> | C4           | 0.50   | 0.50                    |
| [VO(mac <sub>5</sub> )]SO <sub>4</sub> | C5           | 0.25   | 0.25                    |
| Fluconazole                            |              | 0.125  | 0.125                   |



**Fig3: Comparison of MIC of complexes with standard antifungal flucanozole**

## 4. CONCLUSION

The spectral data show that condensation of 1,8-diaminonaphthalene and substituted  $\beta$ -diketones is achieved by the template effect of oxovanadium(IV) ion in aqueous methanol medium. The infrared data show that ligands act as N<sub>4</sub> chelating agents, bonded with all four azomethine nitrogen atoms to the oxovanadium(IV) ion. On the basis of elemental analyses, conductance measurements, magnetic moments and infrared, electronic and EPR spectroscopic technique it is proposed that all the oxovanadium(IV) complexes are square pyramidal wherein presence of oxovanadium(IV) centre is also supported by EPR studies. All the complexes showed good antibacterial and antifungal activity but moderate as compared to standard drug tetracycline and fuconazole. The presence of electron withdrawing groups increased the antimicrobial activity of complexes.

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## 5.1 Abbreviations

DMF-N,N dimethylformamide, DMSO-dimethyl sulfoxide, B.M. Bohr Mangeton, IR-Infrared, EPR- Electron paramagnetic resonance, MIC-Minimum Inhibitory Concentration, MTCC- Microbial Type Culture Collection SDA-Sabouraud Dextrose Agar, DOTA-tetraazacyclododecane tetraacetic acid.

## 6. AUTHOR CONTRIBUTION STATEMENT

J.K.Panday conceptualized and designed the study and Harikesh Kumar did all the experiments, curated the data and prepared the original draft. Ashutosh Singh provided valuable inputs towards designing of the manuscript. All authors discussed the methodology and results and contributed to the final manuscript.

## 7. CONFLICT OF INTEREST

Conflict of interest declared none.

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