

# OXOVANADIUM (IV) MIXED CHELATES CONTAINING POLY (1-PYRAZOLYL) BORATE AND $\beta$ -DIKETONATE LIGANDS: SYNTHESIS, INFRARED CHARACTERIZATION AND MOLECULAR DOCKING STUDIES WITH *XANTHOMONAS AXONOPODIS*

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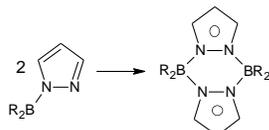
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**ABSTRACT:** Oxovanadium (IV) mixed ligand complexes were prepared from  $\text{VOSO}_4$  obtained by reduction of  $\text{V}_2\text{O}_5$  in ethanolic sulphuric acid. The melting point and solubility of the complexes were determined. Infra-red spectroscopy was used for the characterization of the complexes. Molecular docking studies of the chelated metal complexes were performed with *Xanthomonas axonopodis* using Patchdock molecular docking algorithm server. Binding free energy function based on the atomic contact energy was estimated. The best scoring function gave atomic constant energy of -160.28, -227.12, -266.72, -216.13 Kcal/mole for oxovanadiumbis(acetylacetonate), oxovanadium hexafluoroacetylacetonate/poly(1-pyrazolyl)borate, oxovanadiumbis(poly(1-pyrazolyl)borate and oxovanadium trifluoroacetylacetonate /bis(poly(1-pyrazolyl)borate chelate complexes respectively. Negative values of the binding energy indicated that the use of the synthesized metal complexes for *Xanthomonas axonopodis* eradication would be feasible. On the basis of infrared spectral data, square pyramidal (5-coordinate) structure have been proposed for the metal complexes.

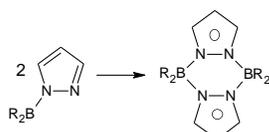
**Keywords:** Oxovanadium, poly (1-pyrazolyl) borate, complexes, Infra-red spectroscopy, molecular docking

## INTRODUCTION

In 1967, Trofimenko<sup>1</sup> reported the study of boron pyrazole chemistry, which dealt with the compounds containing boron bonded to nitrogen of a pyrazole nucleus. He attributed this chemistry to the formation of 1-borylpyrazole fragment which may be stabilized either by dimerisation to form pyrazole - a neutral heterocyclic compound (Scheme 1) whose reactions are organic in nature, or the coordination of a pyrazolide ion (Scheme 2) to form poly (1-pyrazolyl) borate ligands, which exhibited unusual hydrolytic and oxidative stability. They were excellent chelating agents for transition metal cations.

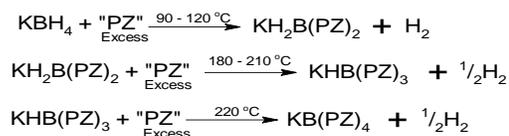


Scheme 1: Dimerization to form pyrazole - a neutral heterocyclic compound. Where R = H or Alkyl group



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Later in 1967, Trofimenko published experimental details for the preparation of poly (1-pyrazolyl) borates<sup>2</sup>. The reactions are summarised in the following sequence (Scheme 3)



Scheme 3: preparation of poly(1-pyrazolyl) borates  
Where "PZ" is used to designate the 1-pyrazolyl fragment

The structures of these salts were proven by the stoichiometry of hydrogen evolution, elemental analysis, infrared and NMR (<sup>1</sup>H and <sup>11</sup>B) spectroscopy. Complexes of these ligands with the divalent cations of the first row transition metals have been synthesized<sup>2</sup>. These complexes, like the  $\beta$ -diketonate ions are of the type:  $\text{R}_2(\text{BPZ}_2)\text{M}$  (M = first row transition series). Because of the much greater steric requirements of the  $\text{B}_2\text{BPZ}_2^-$  ligands, such complexes are always strictly monomeric. For steric reasons, no tris complex is known<sup>3</sup>. Dimeric complexes of

$\text{Cu}^{2+}$  have been prepared and reported with a pyrazole ring symmetrically bridging to metal ions<sup>4</sup>. The transition metal poly (1-pyrazolyl) borate complexes are all insoluble in water. Their solubility products at 25°C are of the order  $10^{-14}$ . The complexes are soluble in acetone and chlorinated hydrocarbons. In the solid state the chelates are stable to air and moisture for years with the exception of the air sensitive  $\text{Mn}(\text{H}_2\text{B}(\text{PZ})_2)_2$  and  $\text{Fe}(\text{H}_2\text{B}(\text{PZ})_2)_2$ . Jozorek<sup>4</sup> has cited thermodynamic evidence to show that the "tris" and "tetrakis" chelates of copper are actually four or five coordinate in contrast to the conclusions reached by Jesson et al and Trofimenko<sup>2</sup>. The thermal stability of the transition metal chelates have been determined by thermo gravimetric analysis<sup>4</sup>. They are all thermally stable below temperature of at least 150 °C<sup>4</sup>.

The Chemistry of V (IV) is dominated by the formation of the oxo species and a wide range of compounds with  $\text{VO}^{2+}$  are known. Of the many oxometal species known, the most stable are the  $\text{VO}^{2+}$  ion. In an extensive review of the  $\text{VO}^{2+}$ , Selbin<sup>5</sup> has concluded that the species is probably the most stable diatomic ion known. It forms a variety of stable complexes which may be cationic, neutral or anionic. Many of the physicochemical properties of this ion are of great interest, notably its electronic spectrum and other properties associated with the configuration.

*Xanthomonas axonopodis* are proteobacteria and as with all proteobacteria they have a gram negative wall consisting of an outer membrane made up of lipopolysaccharide (LPS) and a phospholipid inner membrane<sup>6</sup>. Their appearances are aerobic rod shaped with polar flagella. The leaves, stem and fruits that are infected with *Xanthomonas axonopodis* display lesions which take on yellow halo or ring shaped appearances. They are so persistent that whole orchards have to be destroyed if *Xanthomonas axonopodis* are present<sup>7</sup>. *Xanthomonas* are exclusively pathogenic to a large group of plants such as citrus trees, rice, cotton, beans and grapes. They cause a highly contagious disease called citrus canker. Citrus canker can destroy an entire crop yield, but does not pose any danger to humans or animals. The infection has a wide range of effects which include: defoliation, dieback, severely blemished fruit, reduced fruit quality and premature fruit drop<sup>8</sup>.

This study was therefore undertaken to characterise oxovanadium (IV) complexes containing poly (1-pyrazolyl) borate and  $\beta$ -diketonate ligands. Our interest arose from the similarity of  $\beta$ -diketonate and poly (1-pyrazolate)

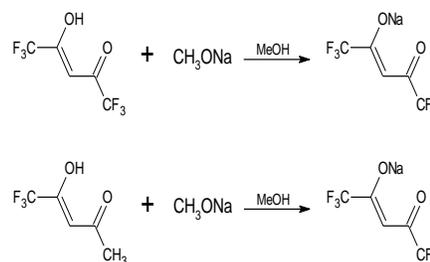
borate. It is of interest to see the effect the two classes of ligands have on the stereochemistry of the complex particularly on the  $\nu(\text{V}=\text{O})$  stretching frequency of the oxovanadium (IV) ion.

## EXPERIMENTAL

Except for the poly (1-pyrazolyl) borates that were obtained from Colombia Organic Chemicals Co. Inc. Manufacturing and Research Chemists Columbia S.C., all other chemicals used were obtained from the British Drug House (BDH) Chemicals Co. Ltd. Poole England. All the chemicals were used without further purification. The melting points of all the complexes were determined using electro thermal melting point apparatus. The infrared spectra for the complexes were recorded in KBr disc using Pyeunicam Sp 2000 infrared spectrophotometer at the department of chemistry, University of Ilorin, Nigeria.

### *Synthesis of the sodium salt of hexafluoroacetylacetonone (HFAC) and trifluoroacetylacetonone (TFAC)*

10g of HFAC (0.0481) was dissolved in minimum amount of methanol and added with stirring to a solution of 2.597g (0.0481 mole) sodium methoxide in methanol. The reaction mixture was transferred into a round bottom flask concentrated under reduced pressure. The yellow powdery product was dried overnight in a vacuum oven at 40°C. The sodium salt of TFAC was prepared similarly with a slight excess of sodium methoxide. Equations of reaction are shown in Scheme 4.



Scheme 4: Synthesis of Sodium salt of hexafluoroacetylacetonone (HFAC) and trifluoroacetylacetonone (TFAC)

### *Synthesis of oxovanadium acetylacetonates complexes*

5.0 g of  $\text{V}_2\text{O}_5$  was added to a solution containing 12  $\text{cm}^3$  of distilled water, 9  $\text{cm}^3$  of conc.  $\text{H}_2\text{SO}_4$  and 25  $\text{cm}^3$  of ethanol. The mixture was then heated on a hot plate in a fume hood. As the reaction proceeded, the colour changed from green to dark blue in which the reduction of  $\text{V}_2\text{O}_5$  to  $\text{VO}^{2+}$  was completed (about 30 minutes). The solution was then

filtered hot and 13 cm<sup>3</sup> of acetylacetone was added to the filtrate. A solution of 20 g Na<sub>2</sub>CO<sub>3</sub> in 125 cm<sup>3</sup> of distilled water was finally added. The precipitate was then filtered using Buckner flask, washed several times with distilled water and dried by drawing air through the filter cake. The product was finally recrystallized in chloroform and kept in a dessicator over CaCl<sub>2</sub>.

### Synthesis of mixed ligand chelates

5.0 g of V<sub>2</sub>O<sub>5</sub> was added to a solution containing 12 cm<sup>3</sup> of distilled water, 9 cm<sup>3</sup> of conc. H<sub>2</sub>SO<sub>4</sub> and 25 cm<sup>3</sup> of ethanol. The mixture was then heated on a hot plate in a fume hood. As the reaction proceeded, the colour changed from green to dark blue in which the reduction of V<sub>2</sub>O<sub>5</sub> to VO<sup>2+</sup> was completed (about 30 minutes). The solution was then filtered hot. Equal moles of corresponding chelating agents (HFAC/KH<sub>2</sub>BPZ<sub>2</sub>, H<sub>2</sub>BPZ<sub>2</sub>/H<sub>2</sub>BPZ<sub>2</sub>, TFAC/H<sub>2</sub>BPZ<sub>2</sub>) were added to the filtrate. A solution of 20 g Na<sub>2</sub>CO<sub>3</sub> in 125 cm<sup>3</sup> of distilled water was finally added. The precipitate was then filtered using Buckner flask, washed several times with distilled water and dried by drawing air through the filter cake. The product was finally recrystallized in chloroform and kept in a desiccator over CaCl<sub>2</sub>.

Structural drawings of the chelated metal complexes were performed with ACD Lab Chem Sketch software. They were saved as PDB file (Figure 1) using Argus lab software<sup>9</sup>. PDB file of *Xanthomonas axonopodis* was downloaded from protein data bank (3KSX) Figure 2. Molecular docking was performed using Patchdock Molecular Docking Algorithm server<sup>10,11</sup>

## RESULTS AND DISCUSSION

All the complexes were powdery, coloured and stable. The colours of the complexes ranged from grey to green. The colours and the melting points of the complexes are shown in Table 1. The complexes are insoluble in water but partially soluble in common organic solvents like acetone, chloroform, methanol, acetonitrile, benzene and toluene.

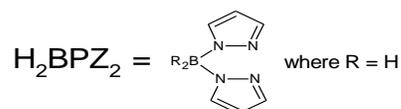
**Table 1: Colour and melting points of the complexes**

Complex	Colour	Melting point °C
[VO(ACAC) <sub>2</sub> ]	Green	178 - 180
[VO(HFAC/H <sub>2</sub> BPZ <sub>2</sub> )]	Grey	275 - 277
[VO(H <sub>2</sub> BPZ <sub>2</sub> ) <sub>2</sub> ]	Yellowish green	79 - 80
[VO(TFAC/H <sub>2</sub> BPZ <sub>2</sub> )]	Grey	168 - 172

ACAC=Acetylacetonate ion,

TFAC = trifluoroacetylacetonate ion, HFAC

=hexafluoroacetylacetonate ion,



The infrared spectra of all the complexes were very similar thus implying that the complexes have similar structures. The frequencies of the observed bands are reported in Table 2.

**Table 2: Infrared frequencies (cm<sup>-1</sup>) of the major observed bands**

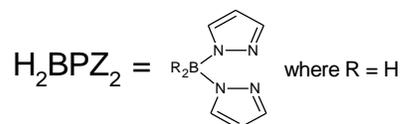
[VO(ACAC) <sub>2</sub> ]	[VO(HFAC/H <sub>2</sub> BPZ <sub>2</sub> )]	[VO(H <sub>2</sub> BPZ <sub>2</sub> ) <sub>2</sub> ]	[VO(TFAC/H <sub>2</sub> BPZ <sub>2</sub> )]
3450 w,br	3140, w,br	2400,s	2900,s
2740 w,br	2720,w,s	2300,s	2720, w
2450 w,br	2500,w,br	1950,m	2480, w
2000 w	1880,w,br	1735,m	1750, vw
1600 w, s	1680,w	1635,w	1625, s
1535 m, s	1645,m	15455,s	1590, vw
1290 m, s	1495,m	1495, s	1530,w
1160 w, br	1310,s	1295,s	1505,m
1020 m, s	1255,m	1210,s	1465,vs
1000 m,s	1210,s	1185,s	1310,s
940 m,s	1150,s	1160,vs	1290,s
855 w, br	1110,s	1140,vs	1210,s
800 m, br	1050,s	1075,s	1150,s
790 m, br	920,s	1018,s	1120,m
720 m, s	890,s	1005,m	1095,w
690 m,s	850, vw	970,s	985,m
660 vw, s	810, w	950,s	1050,vs
610 m,s	790,s	915,m	985,m
560 vw,s	655,m	895,s	975,s
490 m,s	615,m	860,s	970,s
465 w,s		770,br	920,w

S=strong, w = weak, vw = very weak, m = medium, br = broad,

ACAC = Acetylacetonate ion, TFAC =

trifluoroacetylacetonate ion, HFAC

=hexafluoroacetylacetonate ion,



For structural elucidation purposes, the most important frequencies are those due to V=O, V-N and V-O stretching vibrations and discussions have been limited to those bands. Assignments have been made by comparison of the

observed frequencies with those of known complexes in literature<sup>12</sup>. Oxo Vanadyl Acetylacetonate complex showed a strong band at  $1000\text{ cm}^{-1}$ . This band has been attributed to  $\nu(\text{V}=\text{O})$  stretching vibration. Generally, there is a lowering of the  $\nu(\text{V}=\text{O})$  stretching frequencies in the pyrazolyl rings ( $970\text{ cm}^{-1}$ ) thus indicating that the nitrogen atoms of the pyrazolyl rings are strongly bound to the  $\text{VO}^{2+}$  centre. The frequencies  $3450\text{ cm}^{-1}$  in the Oxo Vanadyl Acetylacetonate complex indicated the presence of water of crystallization. They are conspicuously absent in the other complexes which indicated the absence of water of hydration. A weak to medium band between  $2400 - 2600\text{ cm}^{-1}$  assignable to  $\nu(\text{B-H})$  mode was observed in HFAC/ $\text{H}_2\text{BPZ}_2$ ,  $\text{H}_2\text{BPZ}_2/\text{H}_2\text{BPZ}_2$  and TFAC/ $\text{H}_2\text{BPZ}_2$  complexes. The mixed ligand complexes showed a weak band in the region  $1690 - 1635\text{ cm}^{-1}$ . This band has been attributed to the  $\nu(\text{C}=\text{N})$  stretching vibration of the pyrazolyl moiety. This band is absent in Oxo Vanadyl Acetylacetonate complex.

The crystal structure of *Xanthomonas axonopodis* presented in Figure while the molecular docking with the metal chelates are presented in Figure 2 – 5. Binding free energy function based on the atomic contact energy was estimated as shown in equation 9<sup>13</sup>.  $\Delta G_{cal} = \Delta E_c + \Delta E_{el} - T\Delta S_{trv}$  (Equation 9) where  $\Delta E_c$  is the change in atomic contact energy.  $\Delta E_{el}$  is the direct electrostatic interaction between protease and its inhibitor. The term  $\Delta S_{trv}$  denotes the entropy change associated with the six degrees of freedom of rotation/translation and vibration<sup>13</sup>. The best scoring function gave atomic constant energy of  $-160.28$ ,  $-227.12$ ,  $-266.72$ ,  $-216.13$  Kcal/mole for oxovanadiumbis (acetylacetonate), oxovanadiumhexafluoroacetylacetonate/poly(1-pyrazolyl)borate, oxovanadiumbis (poly 1pyrazolyl) borate and Oxo Vanadyl Acetylacetonate/bis (poly(1-pyrazolyl)borate chelate complexes respectively. Negative values of the binding energy indicated that the use of the synthesized metal complexes for *Xanthomonas axonopodis* eradication would be feasible.



Figure 1: X-ray crystallography of *Xanthomonas axonopodis*

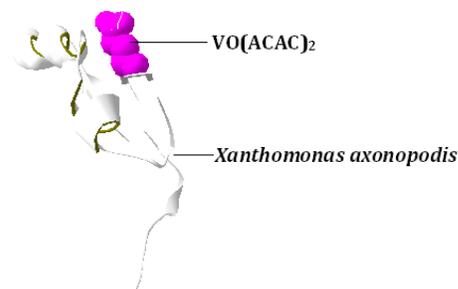


Figure 2:  $\text{VO}(\text{ACAC})_2$  docked with *Xanthomonas axonopodis*  
Atomic contact energy =  $-160.28$  Kcal/mole

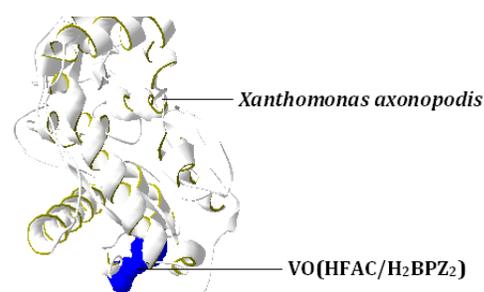


Figure 3:  $\text{VO}(\text{HFAC}/\text{H}_2\text{BPZ}_2)$  docked with *Xanthomonas axonopodis*  
Atomic contact energy =  $-227.12$  Kcal/mole

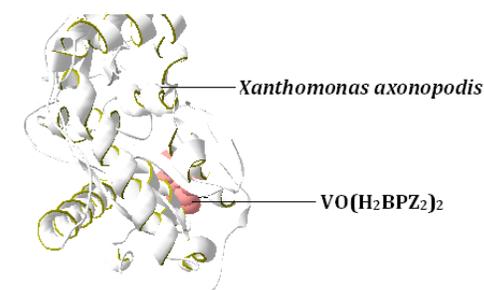


Figure 4:  $\text{VO}(\text{H}_2\text{BPZ}_2)_2$  docked with *Xanthomonas axonopodis*  
Atomic contact energy =  $-266.72$  Kcal/mole

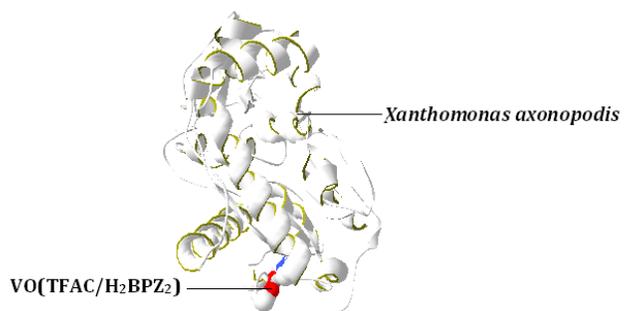


Figure 5:  $\text{VO}(\text{TFAC}/\text{H}_2\text{BPZ}_2)$  docked with *Xanthomonas axonopodis*  
Atomic contact energy =  $-216.13$  Kcal/mole

Thus on the basis of the infrared spectra, square bipyramidal structures have been proposed for the metal chelates. The proposed structures for the complexes are presented in Figures 6 - 9.

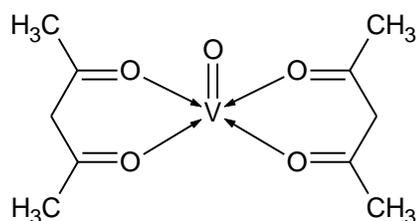


Figure 6: Suggested structure for Oxovanadium Bis(acetylacetonate) chelate complex

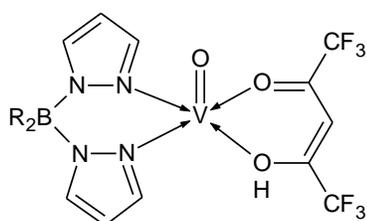


Figure 7: Suggested structure for Oxovanadium hexafluoroacetylacetonate/poly(1-pyrazolyl) borate chelate complex, where R = H

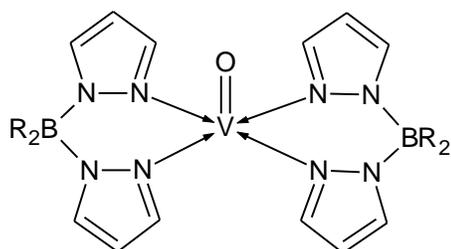


Figure 8: Suggested structure for Oxovanadium Bis(poly(1-pyrazolyl)borate) chelate complex, where R = H

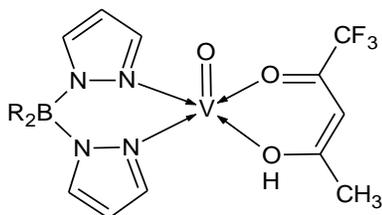


Figure 9: Suggested structure for Oxovanadium trifluoroacetylacetonate/Bis(poly(1-pyrazolyl)borate) chelate complex, where R = H

## Conclusion

This research work showed that poly (1-pyrazolyl) borate ligands formed air stable and coloured complexes with  $VO^{2+}$  species. Most of them are water insoluble but partially soluble in common organic solvents like acetone, methanol, benzene, toluene and chloroform. All the complexes showed infrared absorption characteristics of (V=O) stretching frequencies. Negative values of the binding energy indicated that the use of the synthesized metal complexes for *Xanthomonas Axonopodis* eradication would be feasible. On the basis of infrared, square pyramidal structures were proposed for the chelated metal complexes.

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