

Bidentate Isatin Schiff Base Ligands Oxovanadium (IV) Complexes

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Abstract

The aim of the present study is to synthesize the oxovanadium complex of the V^{3+} ion with isatin Schiff bases. Spectroscopic methods have been used to confirm these models of complexation and to understand the structures of the species formed in methanolic solution. We also have isolated a complex of Vanadium (III) with isatin Schiff bases in the solid phase.

Keywords: Synthesis; Monooxovanadium (IV) ; Isatin ; Ligands

Introduction

Vanadium coordination chemistry constitutes a field of increasing interest and has been the subject of extensive studies during recent decades by many different authors [1,2]. A great number of ligands have been employed in the study of biologically relevant vanadium systems with the aim of finding a possible correlation between activity and coordination geometry. Moreover, diverse aspects related to its biological and pharmacological activities have been reviewed [3,4].

Vanadium (III, IV and V) has a high affinity for N, O and/or S donor groups. It reacts with many naturally occurring species, including pyridine carboxylic acids, forming stable complexes with diverse stoichiometries. Metal complexes of pyridine carboxylic acids and some of their derivatives have recently received considerable attention as model systems for the design of new metallopharmaceutical compounds. Furthermore, several vanadium complexes have been investigated as antidiabetic agents, most of them involving vanadium (IV) as the metal center [5–9]. Among others, oxovanadium (IV) associated with picolinate and other related ligands seem to be very promising as insulin-mimetic oral drugs [7–9].

It was also determined that vanadium complexes of this bio-ligand are more effective than the ligand alone in the treatment of diabetes [10]. The insulin-like properties of the Vanadium (V) dipicolinate compound; [VO₂dipic], originally prepared by Wieghard [11], and its 4-hydroxydipicolinate derivative; [VO₂dipic-OH], have been recently determined [10,12]. The structural chemistry of Vanadium (V), like that of other transition metals in high oxidation states, is mainly related to the oxo complexes. Although a great number of oxo-bridged vanadium (IV and V) and mixed valence complexes are described in the literature, these compounds are less abundant than those of Ti (IV) or Mo (V,VI). Moreover, to our best knowledge, only few examples of bis oxo-bridged compounds have been reported [13–14].

Isatin is an endogenous compound isolated in 1988 and has been reported to possess a wide range of central nervous system activities [15,16]. It has also been found as a metabolic derivative of adrenaline in humans [16]. Various derivatives of isatin are known to possess a range of pharmacological properties including antiprotozoal activities [17]. Within the context of enzyme inhibitors, isatins (also known as 2,3-dioxindoles) have found recent applications in the inhibition of cysteine and serine proteases [18]. Thus isatin is a biologically validated starting point for the design and synthesis of chemical libraries directed at these targets [19].

Various derivatives of isatin are known to possess a wide range of pharmacological properties such as antibacterial [20], antifungal [21], antiviral [22], anti-HIV [23], and cytotoxic activities [24].

The aim of the present study is to synthesize the oxovanadium complex of the V³⁺ ion with isatin Schiff bases. Spectroscopic methods have been used to confirm these models of complexation and to understand the structures of the species formed in methanolic solution. We also have isolated a complex of Vanadium (III) with isatin Schiff bases in the solid phase.

Experimental

Chemicals

All solvents (Sigma/Aldrich) and chemicals were reagent grade and used without further purification. Water was deionized (Barnstead D8902 and D8904 cartridges) and distilled (Corning MP-1 Megapure Still) before use. The yields are for analytically pure compounds with calculations based on the metal ion, where present.

Instruments

Melting points were determined on the Electro-thermal Melting Point apparatus and were uncorrected. Infrared spectra were recorded on the Shimadzu-420 infrared spectrophotometer. $^1\text{H-NMR}$ and $^{13}\text{C NMR}$ spectra were recorded in DMSO- d_6 on Bruker 300 MHz spectrometers (chemical shifts are given in parts per million (PPM)). Elemental analyses (C, H, N) were performed by the Microanalytical Unit.

General procedure for the synthesis of isatin schiff base derivatives

A mixture of isatin (5 mmol) and aromatic or heterocyclic primary amines (5 mmol) are refluxed in ethanol (50 ml) in the presence of acetic acid as the catalyst for 0.5-2 h (Figure 1). After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure and the crude product was washed with water and recrystallized from ethanol to give pure products.

Some synthesized compounds are compared with those reported in earlier literature [20-24].

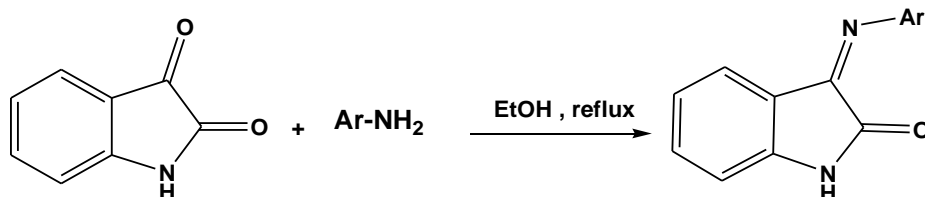


Figure 1. Schematic representations of synthesized isatin schiff bases

2.4. Synthesis of new oxo vanadium compounds

Synthesis and characterization Vanadyl complexes were prepared by addition of 10 ml degassed MeOH or acetone to 0.50 mmol isatin schiff base derivatives while dissolved in MeOH with gentle heating and stirring. Dropwise addition of Vanadyl sulphate [$\text{VO}(\text{SO}_4)$], 0.25 mmol, in 10 ml degassed methanol, followed by reflux for 2-4 h, and then cooling to room temperature (RT), afforded a solid product that was then isolated by vacuum filtration, washed with cold methanol and dried overnight in vacuo at RT (Figure 2).

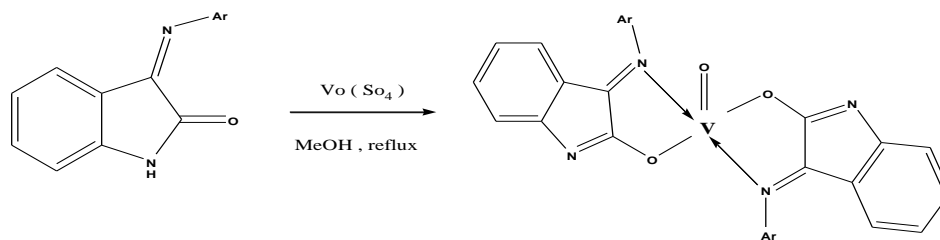
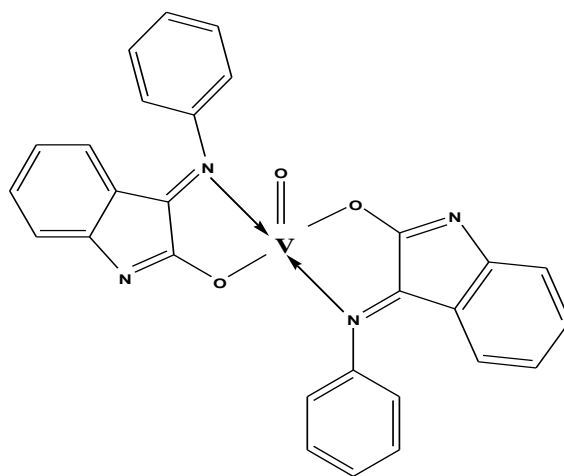


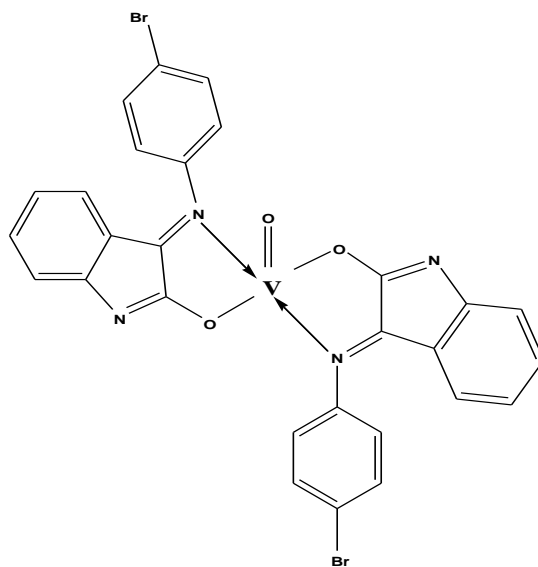
Figure 2. Schematic representation of oxovanadium complexes from isatin schiff base derivatives

Some characteristic data for new compounds are given here:



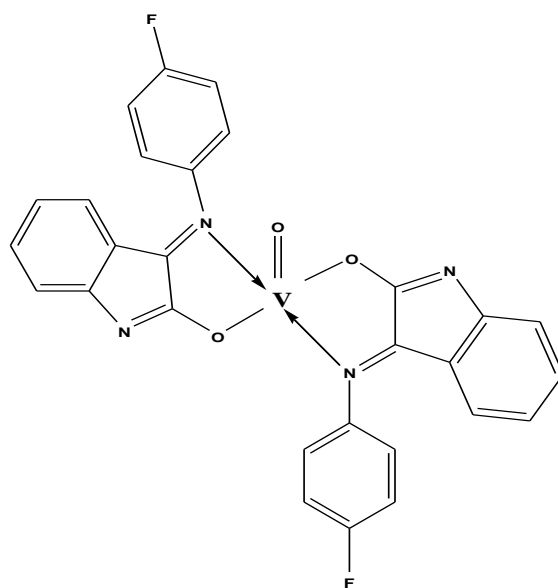
Bis((Z)-3-(phenylimino) indolin-2-one) oxovanadium (IV)

m.p =IR (KBr) Cm^{-1} :3000-3080 C-H(Ph . stretch) ,1600 C=N (stretch) ,1400-1600 C-H (Ph , bend) , 1100-1310 C-O . ^1H NMR (300 MHz, CDCl_3) δ 7.5-7.7 (m, 5 H, Ph) , 6.5 (d, 4H, Ph) 6.2 (d, 4H, Ph). ^{13}C NMR (300 MHz, CDCl_3) δ 120, 125, 126, 128, 133, 136, 151, 155, 167, 169. Elemental analysis for $\text{C}_{31}\text{H}_{26}\text{N}_4\text{O}_3\text{V}$ (MW 533). Calcd: C 67.27, H 4.73, N 10.12, O 8.67, V 9.20. Found: C 67.12, H 4.95, N 10.24, O 8.53, V 9.29.



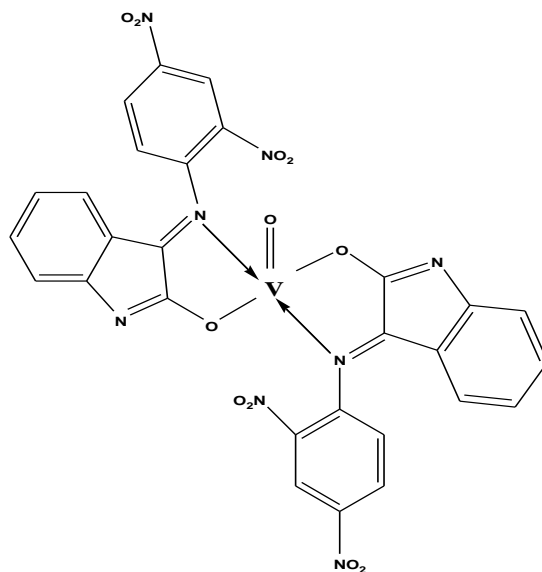
Bis ((Z)-3-(4-bromophenylimino) indolin-2-one) oxovanadium (IV)

m.p =IR (KBr) Cm^{-1} :3000-3100 C-H(Ph . stretch) ,1627 C=N (stretch),1400-1600 C-H (Ph , bend) , 1125-1331 C-O . ^1H NMR (300 MHz, CDCl_3) δ 8.3 (d, 4 H, Ph-Br), 8.2 (d, 4H, Ph-Br), 6.9 (d, 4H) 6.7 (d , 4H , Ph), 0.85 (t, $J = 10.0$ Hz, 6H, Ph) . ^{13}C NMR (300 MHz, CDCl_3) δ 122, 125, 127, 129, 131, 134, 151, 154, 165, 167. Elemental analysis for $\text{C}_{31}\text{H}_{24}\text{Br}_2\text{N}_4\text{O}_3\text{V}$ (MW 711). Calcd: C 52.35, H 3.40, N 7.88, O 6.75, V 7.16, Br 22.47. Found: C 52.44, H 3.31, N 7.99, O 6.55, V 7.28, Br 22.29.



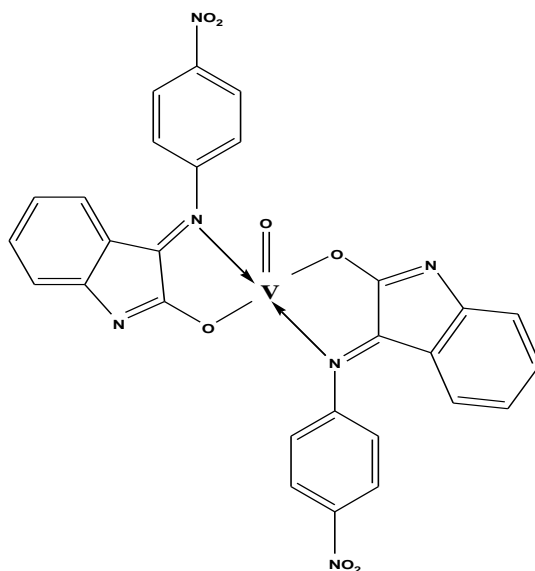
Bis ((Z)-3-(4-fluorophenylimino) indolin-2-one) oxovanadium (IV)

m.p =IR (KBr) Cm^{-1} :2900-3000 C-H(Ph . stretch) ,1616 C=N (stretch),1480-1600 C-H (Ph , bend) , 1085-1249 C-O . ^1H NMR (300 MHz , CDCl_3) δ 7.7 (d, 4 H, Ph-F),7.6 (d, 4H,Ph-F), 7.2 (d, 4H, Ph) 6.9 (d , 4H, Ph). ^{13}C NMR (300 MHz , CDCl_3) δ 117, 122, 123, 125, 129, 133, 152, 166. Elemental analysis for $\text{C}_{31}\text{H}_{24}\text{F}_2\text{N}_4\text{O}_3\text{V}$ (MW 589). Calcd: C 63.16, H 4.10, N 9.50, O 8.14, V 8.64, F 6.45. Found: C 63.28, H 4.35, N 9.36, O 7.89, V 8.71, F 6.34.



Bis ((Z)-3-(2,4-dinitrophenylimino) indolin-2-one) oxovanadium (IV)

m.p =IR (KBr) Cm^{-1} :2925 C-H(Ph . stretch) ,1612 C=N (stretch),1450-1600 C-H (Ph , bend) , 1016-1132 C-O . ^1H NMR (300 MHz , CDCl_3) δ 7.7 (S, 2H, Ph- NO_2), 7.6 (d, 4H,Ph- NO_2), 7.4 (d, 4H, Ph), 7.2-7.1 (d , 4H, Ph). ^{13}C NMR (300 MHz , CDCl_3) δ 121, 125, 126, 128, 129, 132, 133, 145, 153, 154, 164, 166 . Elemental analysis for $\text{C}_{31}\text{H}_{22}\text{N}_8\text{O}_{11}\text{V}$ (MW 733). calcd : C 50.76, H 3.02, N 15.28, O 23.99, V 6.95. Found: C 50.82, H 2.93, N 15.15, O 23.75, V 7.12.



Bis((Z)-3-(4 - nitro phenylimino) indolin-2-one) oxovanadium (IV)

IR (KBr) Cm^{-1} : 2980 C-H(Ph . stretch) , 1600 C=N (stretch) , 1450-1600 C-H (Ph , bend) , 1120-1145 C-O . ^1H NMR (300 MHz , CDCl_3) δ 7.5 (s , 2 H , Ph- NO_2) , 7.3 (d, 4H, Ph- NO_2) , 7.4 (d, 4H, Ph) , 7.2-7.1 (d , 4H, Ph). ^{13}C NMR (300 MHz , CDCl_3) δ 122, 124, 126, 129, 130, 132, 133, 147, 153, 154, 164, 168. Elemental analysis for $\text{C}_{31}\text{H}_{24}\text{N}_6\text{O}_7\text{V}$ (MW 643). Calcd: C 57.86, H 3.76, N 13.06, O 17.40, V 7.92. Found: C 57.54, H 3.61, N 14.75, O 23.95, V 7.22.

Results and discussion

The ligands used in this study are shown in figure 2. They were prepared by condensing isatin and aromatic or heterocyclic primary amines in alcoholic solution. Isatin schiff bases have been chosen for coordinating vanadium due to its ability of stabilizing O-VIV-O-VV-O bonds [25-28]. The organic molecules contain one, two or three tripod tetradentate binding sites that are able to coordinate the same number of vanadium atoms (figure 2). Bis isatin oxovanadium compounds are very hydrophilic and absorb large quantities of water in suspension. The vanadium mixed-valence complexes were prepared by mixing the organic ligand with the appropriate amount of vanadyl sulfate (Vanadium (IV)) and sodium vanadate (Vanadium (V)).

In the IR spectrum of the ligands, the bands at 3100 Cm^{-1} are assigned to N-H stretching frequencies. The carbonyl and azomethine spectral bands are observed at 1630 and 1580 Cm^{-1}

respectively. The band at 1250 Cm^{-1} respectively corresponds to C-O band. The bands in the range $1570\text{--}1325\text{ Cm}^{-1}$ are difficult to assign due to crowding of bands but sharp bands near to $1450\text{--}1600\text{ Cm}^{-1}$ are probably due to the aromatic C-H bands. The IR spectra of the compounds exhibit significant alterations due to coordination of the bidentate ligand with the metal. The assignments done are tentative due to crowding of peaks.

In bis isatin vanadium compound, a medium intensity band observed with splittings at 1500 Cm^{-1} is due to newly formed-N=C-C=N- moiety. The shifting of the C=N band, due to complexation is comparatively less when compared to that of the ligand and is found at 1580 Cm^{-1} . A strong band observed at 1368 Cm^{-1} is assigned to the band. Strong bands are observed in the range $1510\text{--}1420\text{ Cm}^{-1}$. These are attributed to the aromatic ring vibrations. The typical V=O stretching frequencies in oxovanadium complex, appear as medium strong bands at $962,978\text{ Cm}^{-1}$. The stretching vibrations of the V-O and the V-N bond were observed at 453.389 Cm^{-1} .

The ^1H NMR spectral data of the free ligands and complexes are shown as follow. As expected, OH resonances bonding to the aromatic ring and the carboxyl group are absent in the title complexes. A broad NH and OH (δ 10.12, 8.77 ppm) resonances of the free isatin schiff base ligands will be disappeared in the complex structure spectra indicating coordination through the deprotonated hydroxyl group. The peaks at 8.2-8.3 ppm and 6.7-6.9 ppm in complex are attributed to C-H in aromatic primary imine and isatin, respectively. With different substituents in aromatic primary imine, the chemical shift of C-H bands will be shifted to up field or down field zone in ^{13}C NMR spectra, the peaks that are located upper than δ 150, correspond to C-O, C=N, and =C-N bands while the ones located at δ 120-140, correspond to C-Hs of Ph in isatin and aromatic imine group.

Acknowledgment

The authors thank the Medicinal and Natural Products Chemistry Center, Shiraz, Iran and Islamic Azad University, Ahvaz Branch, Iran for their supports in this work.

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