

Vibrational Spectrum of Bis(pyrrolidine-N-carbodithioato)-oxovanadium(IV): A New Insulin-Mimetic Vanadyl Complex

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SUMMARY. It has been recently found that bis(pyrrolidine-N-carbodithioato)-oxovanadium (IV) is an orally active insulin-mimetic complex. In order to facilitate the characterization and rapid identification of this interesting drug, we have recorded its infrared and Raman spectra and made an assignment of its most characteristic bands. On the basis of this analysis some structural peculiarities of the complex are also discussed.

RESUMEN. "Espectro Vibracional de Bis(pirrolidinio-N-carboditioato)oxovanadio (IV): Un Nuevo Complejo Insulino-Mimético de Vanadilo". Recientemente se ha demostrado que el bis(pirrolidinio-N-carboditioato)-oxovanadio (IV) es un complejo con actividad insulino-mimética, administrable oralmente. A efectos de facilitar la caracterización y rápida identificación de esta interesante droga, hemos registrado sus espectros infrarrojo y Raman y realizado la asignación de sus bandas más características y en base a este análisis se discuten algunas peculiaridades estructurales del complejo.

INTRODUCTION

Although the main abnormality in insulin-dependent diabetes mellitus is hyperglycemia due to deficiency of insulin¹, there are many serious secondary complications such as arteriosclerosis, renal disfunctions, cardiac abnormality and ocular disorders. At present, severe diabetes can be only controlled by daily injections of insulin, and thus, the development of compounds that allow insulin replacement or insulin mimetics on oral administration would be very useful^{1,2}.

The finding that blood glucose levels of rats with streptozin (STZ)-induced diabetes are normalized by treatment with different vanadium compounds and complexes has stimulated research on insulin-mimetic vanadium compounds¹⁻⁷.

Recently, Sakurai *et al.*⁸ demonstrated that the complex bis(pyrrolidine-N-carbodithioato)-oxovanadium (IV) (Fig. 1) is very effective for

normalizing both the serum glucose and free fatty acids levels in STZ-rats. When the complex was administered orally or by intraperitoneal injection at a dose of 10 mg V/kg body weight, to Wistar rats with STZ-induced diabetes, the serum glucose level decreased to the normal range within 2 or 3 days, and was maintained in the normal range by daily administration of 5 mg V/kg.

McCormick⁹ reported the preparation of this complex, together with those of other dithiocarbamate compounds in 1968, but they were scarcely characterized. Therefore, and in order to advance in a better characterization of this novel insulin-mimetic agent and to facilitate its rapid identification, we have performed an analysis of its infrared spectrum, complemented with information obtained from the corresponding Raman spectrum.

KEY WORDS: Oxovanadium(IV) complex, Insulin-mimetic activity, IR spectrum, Raman spectrum, Structural characteristics.

PALABRAS CLAVE: Complejo de oxovanadio(IV), Actividad insulino-mimética, Espectro IR, Espectro Raman, Características estructurales.

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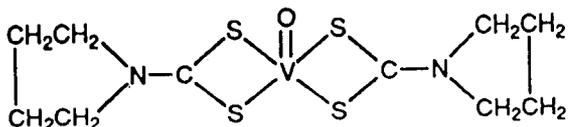


Figure 1. Schematic structure of the complex

EXPERIMENTAL

Synthesis of the complex

Ammonium pyrrolidine-N-carbodithioate was prepared by reaction of pyrrolidine, carbon disulfide and ammonium hydroxide in absolute ethanol. It was purified by reprecipitation from methanol with diethyl ether/ethanol mixtures. 0.04 mol of this compound were dissolved in a 50% ethanol/water solution. On the other hand, 0.02 mol of $\text{VOSO}_4 \cdot 5\text{H}_2\text{O}$ were dissolved in 25 ml of warm water, to which 25 ml of ethanol were added after dissolution of the sulfate had taken place. Finally, the vanadyl solution was dropwise added to that of the ligand under vigorous stirring whereupon a pale, gray greenish precipitate was formed. After filtration, the precipitated complex was washed with 300 ml of distilled water and with small portions of ethanol and diethyl ether and dried in vacuum over P_4O_{10} for two days⁹. The yield was 90%. The complex was stored under vacuum in a freezer.

Spectroscopic measurements

The infrared spectra of the pure ligand and that of the complex were recorded with a Perkin Elmer 580 B spectrophotometer, using the KBr pellet technique. Raman spectra were obtained with a Bruker IFS 66 FTIR instrument provided with a FRA 106 Raman accessory. The samples were excited with the 1064 nm line of a solid state Nd:YAG laser.

RESULTS AND DISCUSSION

The infrared and Raman spectra of the complex, in the spectral range between 1600 and 250 cm^{-1} , are shown in Figures 2 and 3, respectively. The assignment proposed for the most characteristic bands of the full spectra is presented in Table 1 and briefly commented as follows:

a) The stretching vibrations of the CH_2 -groups (not shown in Figures 1 and 2) appear as well defined and strong bands in both spectra, and lie clearly in the range which is characteristic for these modes in a ring structure¹⁰.

b) Some deformational modes of the same groups could also be identified in the usual ranges for this type of vibrations¹⁰. All these bands are slightly displaced after complexation, indicating an influence of the metal-to-ligand bonding on the ring bond characteristics. In the

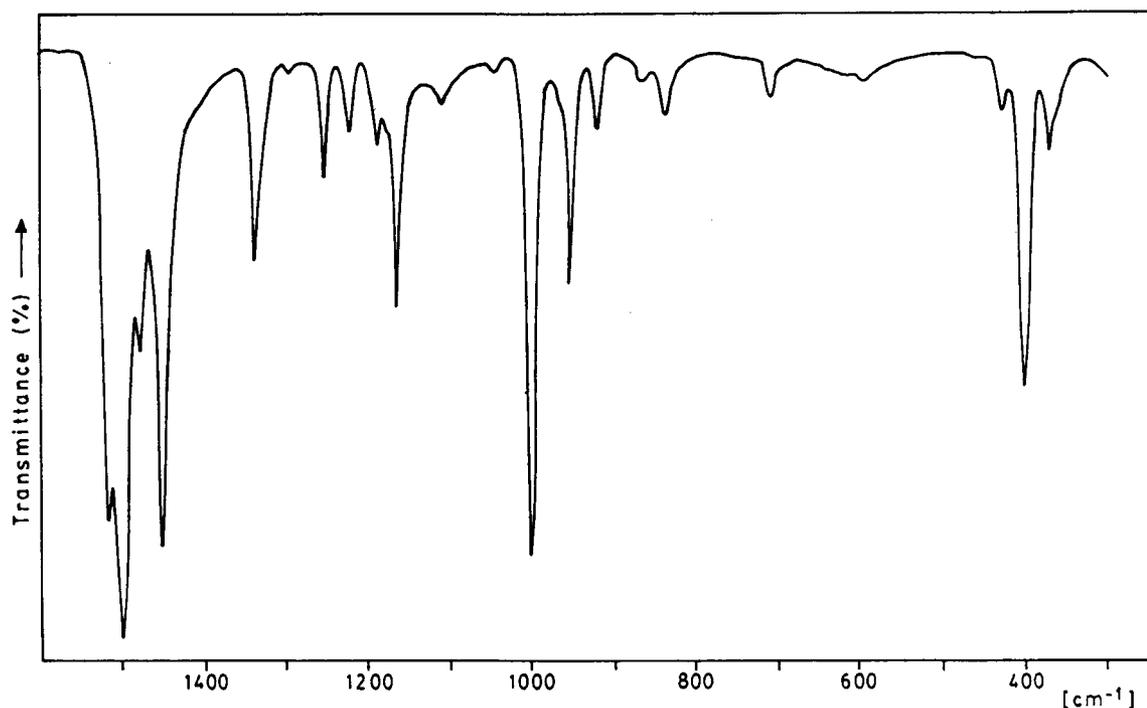


Figure 2. Infrared spectrum of the complex, in the range between 1600 and 250 cm^{-1} .

Infrared (cm ⁻¹)	Raman (cm ⁻¹)	Assignment
2972 vs	2980 s	
	2923 s	v(CH ₂)
2870 vs	2875 s	
1512 m, 1494 vs	1518 m, 1498 s	v(C-N)
1473 w, 1446 vs	1475 w, 1450 s	δ(CH ₂)
1333 s	1337 s	ring "breathing"
1290 vw	---	
1249 m	1251 s	δ(CH ₂)
1220 m	---	δ(CH ₂)
1183 w	1173 m	v(C-C)
1159 s	1160 w	v(CNC)ring
---	1137 m	ring "breathing"
1039 w		
992 vs	993 vs	v(V=O)
945 s	943 w	v(C-C)
914 m	915 m	ring "breathing"
860 w	---	v(CNC)ring/δ-ring
828 m	830 w	v(C-S)
700 w	698 m	
614 w, 585 w	---	ρ(CH ₂)
---	455 vs	
418 w	420 w	
388 vs	390 m	v(V-S)
359 m	365 w	δ(CNC)ring (?)
349 sh		

Table 1. Assignment of the vibrational spectrum of the investigated complex. vs: very strong; s: strong; m: medium; w: weak; vw: very weak; sh: shoulder.

free ligand these bands are found at 1470 (vw), 1450 (w), 1243 (s) and 1212 (m) cm⁻¹, respectively.

c) Ring "breathing" modes as well as stretching vibrations of the C-N-C moieties of the pyrrolidine ring and skeletal v(C-C) modes were tentatively assigned on the basis of some general literature references^{10,11}.

d) A very interesting mode in this type of complexes is the C-N stretching vibration involving the N atom and the C atom of the CS₂ moiety, usually called "thioureide band", which frequency is usually intermediate between that of a simple C-N and a double C=N bond^{9,12}. In the present case, this band is found at 1494 cm⁻¹ in the IR spectrum and at 1498 cm⁻¹ in the Raman spectrum. Its doublet structure can be probably related to correlation field effects. In the free ligand this band is located at 1412 (IR) and 1420 (Raman) cm⁻¹, clearly showing a reinforcement of this bond after complex formation.

e) The v(C-S) stretching mode is found as a unique band, located at 828 cm⁻¹ in the IR spectrum (830 cm⁻¹ in the Raman spectrum), as it is expected for a dithiocarbamate complex with bidentate coordination^{12,13}.

f) The characteristic v(V=O) stretching vibration could be clearly identified in both spectra, in which it appears as a very strong band. On the other hand, the typical v(V-S) mode, related to the metal-to-ligand vibration, is also found in the expected range¹³.

Some general comments on the structural characteristic of the investigated complex can be made on the basis of the commented spectroscopic results. As stated earlier⁹, one can admit for it a tetragonal-pyramidal structure, with C_{4v}

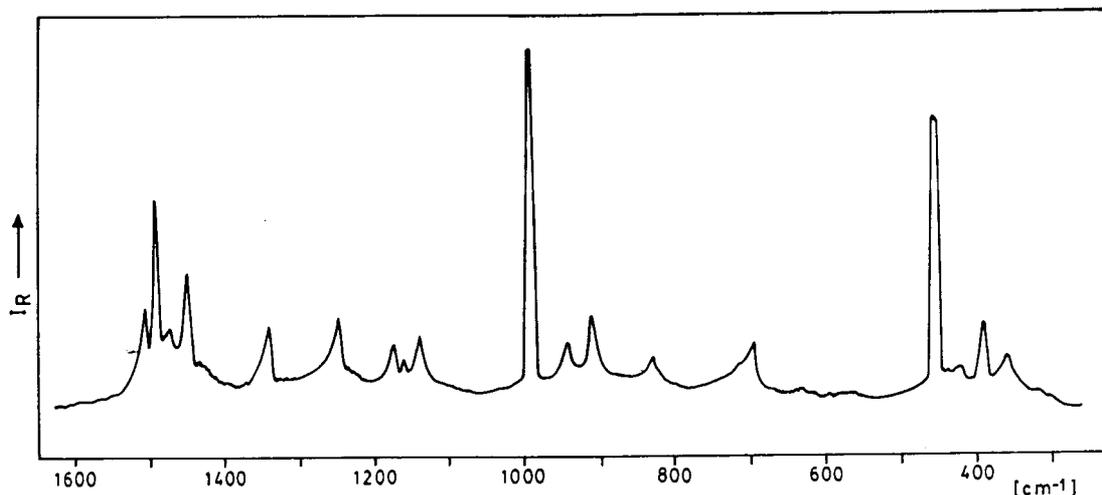


Figure 3. Raman spectrum of the complex, in the range between 1600 and 250 cm⁻¹.

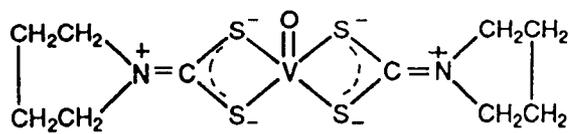


Figure 4. Suggested canonical form that predominates in the structure of the complex.

symmetry, similar to that of the well known oxovanadium(IV) acetylacetonate complex, $\text{VO}(\text{acac})_2$ ¹⁴.

The suspected possible dimerization of the complex in the solid state, with generation of *trans* O=V-S bonds⁹, can be definitively excluded on the basis of the position of the $\nu(\text{V}=\text{O})$

stretching mode. In the case of the generation of such dimeric (or polymeric) oxovanadium (IV) species this mode always lies below 900 cm^{-1} (cf. refer^{15,16} and references therein).

Finally, the behaviour of the $\nu(\text{C}-\text{N})$ "thioureide"-band confirms⁹ the important contributions of the canonical form shown in Fig. 4 on the overall complex structure.

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