



# Vibrational spectra of bis(maltolato)oxovanadium(IV): A potent insulin mimetic agent

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## ABSTRACT

The FTIR and FT-Raman spectra of the oxovanadium(IV) complex of 3-hydroxy-2-methyl-4-pyrone (maltol) bis(maltolato)oxovanadium(IV) were recorded and briefly discussed by comparison with the spectra of uncoordinated maltol and with some related species.

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## 1. Introduction

An important number of simple and complex vanadium compounds present a wide and interesting spectrum of biological and pharmacological activities [1–4]. In recent years the studies on pharmacological applications of vanadium were essentially centered in compounds with insulino-mimetic [2,5–9] and antitumoral activities [2,9–12], and different interesting and promising results have been obtained with some of them [3,9].

Bis(maltolato)oxovanadium(IV) (BMOV, Fig. 1) [13], is so far considered as the most potent insulino-mimetic vanadium-containing complex *in vivo* [14]. The first human clinical trials (Phase I and Phase IIa) were completed recently with its ethylmaltol analog, bis(ethylmaltolato)oxovanadium(IV), showing promising results [14,15].

Despite the fact that an important number of studies have been performed with BMOV [14,16,17], its vibrational-spectroscopic behavior has never been analyzed and discussed in detail. In order to fill this gap and contribute to a wider characterization of this interesting metallopharmaceutical we have now investigated its infrared and Raman spectra.

## 2. Experimental

Maltol, 3-hydroxy-2-methyl-4-pyrone, was purchased from Aldrich whereas  $\text{VOSO}_4 \cdot 5\text{H}_2\text{O}$  was from Merck and both reagents were used as purchased.

The complex, BMOV, was prepared as described by Caravan et al. [16], as follows: vanadyl sulfate (2.53 g, 10 mmol) was dissolved in 100 mL of hot distilled water and maltol (2.95 g, 20 mmol) was slowly added. Using a pH-meter, 1N NaOH was added dropwise and with stirring to this solution until the pH reached a value of about 8.5. The resulting mixture was refluxed overnight, and upon cooling to room temperature a birefringent purple/green solid was collected by filtration and washed repeatedly with small portions of cold water. Finally it was dried *in vacuo*. Anal.: Calculated for  $\text{C}_{12}\text{H}_{10}\text{O}_7\text{V}$ , C: 45.45; H: 3.18; V: 16.09%. Found, C: 45.40; H: 3.25; V: 16.1%.

The infrared spectra in the spectral range between 4000 and  $400\text{ cm}^{-1}$  were recorded as KBr pellets with a FTIR-Bruker-EQUINOX-55 spectrophotometer. A total of 40 scans were accumulated. Raman spectra, in the range  $4000\text{--}100\text{ cm}^{-1}$  were obtained with the FRA 106 Raman accessory of a Bruker IFS 66 FTIR instrument. A total of 60 scans were accumulated, using the 1064-nm line of a solid state Nd:YAG laser for excitation. Spectral resolution was  $\pm 4\text{ cm}^{-1}$  in both measurements.

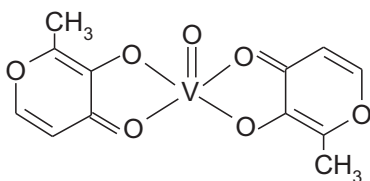
## 3. Results and discussion

### 3.1. Structural characteristics of the complex

Bis(maltolato)oxovanadium(IV), BMOV, crystallizes in the monoclinic  $P2_1/n$  space group with  $Z=4$ . The coordination geometry of the complex is a  $\text{O}=\text{V}(\text{O})_4$  square pyramid with the four O-atoms from the two maltolato ligands constituting the base ( $\text{V}\text{--}\text{O}$  distances between 1.958(8) and 2.024(8) Å) and the oxo-ligand ( $\text{V}=\text{O}$  distance 1.596(7) Å) occupying the apical position. The complex

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**Fig. 1.** Schematic representation of the structure of bis(maltolato)oxovanadium(IV), BMOV.

moiety is present in the *trans–trans* structure [16]. A recent theoretical study of the molecular structure of the complex confirmed that the *trans–trans* structure is that of lowest energy and also reproduces very well all the experimentally determined V–O distances [18].

### 3.2. Infrared and Raman spectra

We have measured the FTIR and FT-Raman spectra of the BMOV complex, and for comparative purposes, also those of “free” uncoordinated maltol. The spectra of the complex in the most interesting spectral range, between 1800 and 400  $\text{cm}^{-1}$ , are shown in Fig. 2 and the proposed assignment is presented in Table 1. This assignment is based on a previous experimental and theoretical study, in the spectroscopic range between 1700 and 1300  $\text{cm}^{-1}$ , of the structure modification of maltol upon anion and cation formation [19], as well as on studies on  $\alpha$ - and  $\gamma$ -pyrones [20,21], complemented with the information provided by standard references [22,23].

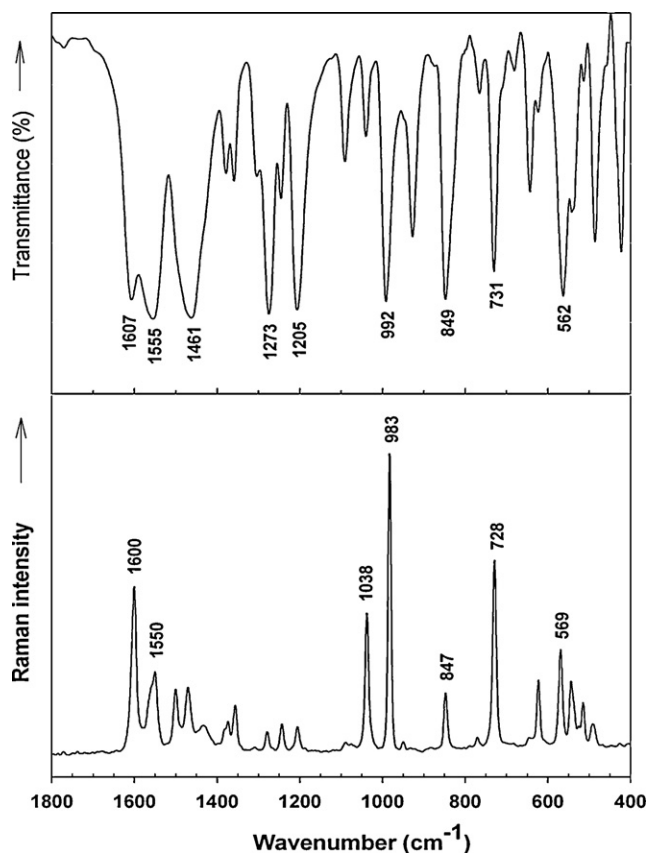
The proposed assignment can be briefly analyzed and discussed, as follows:

- Two of the most characteristic bands of “free” maltol, i.e., the  $\nu(\text{O–H})$  stretching vibration, found as a very strong IR band at 3260  $\text{cm}^{-1}$ , and the  $\delta(\text{C–OH})$  vibration, seen as a very weak feature at 1324  $\text{cm}^{-1}$  in the IR and at 1290  $\text{cm}^{-1}$  in the Raman spectra, are, obviously, absent in the spectra of the complex.
- The origin of the three very strong IR bands of the complex (1607, 1555 and 1461  $\text{cm}^{-1}$ ) is especially interesting and its assignment can be performed by comparison with the known data for mal-

**Table 1**  
Assignment of the infrared and Raman spectra of BMOV (band positions in  $\text{cm}^{-1}$ ).

| Infrared        | Raman           | Assignment  |
|-----------------|-----------------|---|
| 3120 w, 3068 m  | 3116 vw, 3071 w | $\nu(\text{CH})$  |
| 2920 w          | 2932 m          | $\nu(\text{CH}_3)$  |
| 1607 vs         | 1600 s          | $\nu(\text{C=O})$   |
| 1555 vs         | 1550 m          | $\nu(\text{C=C})$   |
| 1461 vs         | 1500 m, 1470 m  | $\nu(\text{C=C}) + \nu(\text{C–O}^-) + \delta_{\text{as}}(\text{CH}_3)$ |
|                 | 1432 w          | $\nu(\text{C–C})$   |
| 1378 m          | 1374 w          | $\delta_{\text{as}}(\text{CH}_3)$                                       |
| 1358 m          | 1357 m          | $\delta_{\text{s}}(\text{CH}_3)$  |
| 1263 w, 1273 vs | 1288 w          | $\delta(\text{CH})$   |
| 1245 m, 1205 vs | 1245 w, 1207 w  | $\delta(\text{CH})$   |
| 1091 m, 1040 m  | 1088 vw, 1038 s | $\nu_{\text{as}}(\text{C–O–C}) + \nu_{\text{ring}}$                     |
| 992 vs          | 983 vs          | $\nu(\text{V=O})$   |
| 940 vw, 927 s   | 948 vw          | $\nu_{\text{s}}(\text{C–O–C})$  |
| 849 vs, 838 sh  | 847 m           | $\gamma(\text{CH})$   |
| 799 m           | 769 vw          | $\gamma(\text{C=O})$  |
| 731 vs          | 728 s           | $\nu(\text{C–C})$   |
| 685 w, 676 w    |                 | $\delta_{\text{ring}}$  |
| 642 s, 623 m    | 638 vw, 622 m   | $\delta_{\text{ring}}$  |
| 562 vs, 550 w   | 569 m           | $\delta_{\text{ring}}$  |
| 540 s           | 543 m           | $\delta_{\text{ring}}$  |
| 513 m           | 515 m           | $\delta(\text{C–O–C})$  |
| 487 vs          | 490 w           | $\nu(\text{V–O})$   |
| 455 w           |                 | $\delta(\text{C=O})$  |
| 419 vs          |                 | $\gamma_{\text{ring}}$  |

vs, very strong; s, strong; m, medium; w, weak; vw, very weak; sh, shoulder.



**Fig. 2.** FTIR (above) and FT-Raman (below) spectra of BMOV, in the spectral range between 1800 and 400  $\text{cm}^{-1}$ .

- The first of them can be related to the  $\nu(\text{C=O})$  stretching, which lies at 1630  $\text{cm}^{-1}$  in “free” maltol and at 1615  $\text{cm}^{-1}$  in its anion.
- The 1555  $\text{cm}^{-1}$  IR band mainly involves the stretching of the C=C bond located at the opposite side of the  $\text{H}_3\text{C–C=C–O}^-$  moiety. In the IR spectrum of the free ligand this band is found at 1569  $\text{cm}^{-1}$  whereas in the anion it lies at 1576  $\text{cm}^{-1}$ .
- The third of these bands (1461  $\text{cm}^{-1}$ ), which is relatively broad and shows a certain asymmetry has a more complex origin. Its Raman counterpart is seen as a medium intensity doublet with components at 1500 and 1470  $\text{cm}^{-1}$ . These bands involve the C=C double bond corresponding to the  $\text{H}_3\text{C–C=C–O}^-$  moiety displaced to lower frequencies after complex formation, one of the  $\delta_{\text{as}}(\text{CH}_3)$  motions (seen at 1459  $\text{cm}^{-1}$  in the “free” ligand) and the  $\nu(\text{C–O}^-)$  vibration (seen at 1419  $\text{cm}^{-1}$  in “free” maltol and at 1513  $\text{cm}^{-1}$  in its anion).
- The two stretching vibrations of the C–O–C moiety lie in ranges which are comparable to those found in  $\gamma$ -pyrone [21].
- The strongest Raman line of free maltol (703  $\text{cm}^{-1}$ ) found also as a strong signal in the complex at 728  $\text{cm}^{-1}$  may be related to a  $\nu(\text{C–C})$  motion but may also be of complex origin, involving one of the ring modes [21].
- Bands related to the oxovanadium(IV) center were relatively easy to identify. The characteristic  $\nu(\text{V=O})$  stretching band is clearly found in the expected range [24,25]. It is seen as the strongest line in the Raman spectrum (983  $\text{cm}^{-1}$ ) and also its IR counterpart (992  $\text{cm}^{-1}$ ) is a very strong and well-defined band. One of the metal–ligand V–O motions could also be unambiguously identified by comparison of the spectra of the complex with those of the free ligand.

Although an important number of maltol complexes have been prepared and investigated during the last years [26–30], detailed vibrational spectroscopic analyses have not been performed, and only some partial IR spectroscopic data are available for some of them. Interestingly, most of the spectra of these complexes (for example,  $\text{Cu}(\text{maltol})_2$  [27],  $\text{V}(\text{maltol})_3$  [26] or  $\text{Ti}(\text{maltol})_2(\text{OH})_2$  [30] and apparently, also those of  $\text{Fe}(\text{III})$ ,  $\text{Cr}(\text{III})$  and  $\text{Al}(\text{III})$  [29]) retain the typical four band pattern of “free” maltol in the in  $1620\text{--}1450\text{ cm}^{-1}$  range, whereas in the present case the two lower energy bands in this region are found as a unique IR feature. It is evident, that these bands shift accidentally together in the IR spectrum, as suggested by the commented asymmetry of the  $1461\text{ cm}^{-1}$  band, but remain clearly separated in the corresponding Raman spectrum.

Regarding the M–O vibrations, in some trivalent and divalent metal maltolato complexes at least one band was observed in a similar region as that found in BMOV [29], whereas in  $\text{V}(\text{maltol})_3$  one of these vibrations was found at  $722\text{ cm}^{-1}$  [26]. This fact suggests that, eventually, one of the weak or medium IR signals found between  $685$  and  $620\text{ cm}^{-1}$  in the BMOV spectra may also involve such a V–O vibration.

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### References

- [1] N.D. Chasteen, *Struct. Bonding* 53 (1983) 105.
- [2] E.J. Baran, *Acta Farm. Bonaerense* 16 (1997) 43.
- [3] D. Rehder, *Bioinorganic Vanadium Chemistry*, J. Wiley, Chichester, 2008.
- [4] D.C. Crans, J.J. Smee, E. Gaidamauskas, L. Yang, *Chem. Rev.* 104 (2004) 849.
- [5] K.H. Thompson, J.H. McNeill, C. Orvig, *Chem. Rev.* 99 (1999) 2561.
- [6] K.H. Thompson, J.H. McNeill, C. Orvig, in: M.J. Clarke, P.J. Sadler (Eds.), *Metallopharmaceuticals II*, Springer, Berlin, 1999, p. 139.
- [7] Y. Adachi, J. Yoshida, Y. Kodera, A. Katoh, J. Takada, H. Sakurai, *J. Med. Chem.* 49 (2006) 3251.
- [8] Y. Shechter, I. Goldwasser, M. Mironchik, M. Fridkin, D. Gefel, *Coord. Chem. Rev.* 237 (2003) 3.
- [9] D. Rehder, *Inorg. Chem. Commun.* 6 (2003) 604.
- [10] C. Djordjevic, G.L. Wampler, *J. Inorg. Biochem.* 25 (1985) 51.
- [11] C. Djordjevic, in: H. Sigel, A. Sigel (Eds.), *Metal Ions in Biological Systems*, vol. 31, Marcel Dekker, New York, 1995, p. 595.
- [12] P. Köpf-Maier, H. Köpf, in: S.P. Fricker (Ed.), *Metal Compounds in Cancer Therapy*, Chapman & Hall, London, 1994, p. 109.
- [13] J.H. McNeill, V.G. Yuen, H.R. Hoveyda, C. Orvig, *J. Med. Chem.* 35 (1992) 1489.
- [14] K.H. Thompson, C. Orvig, *J. Inorg. Biochem.* 100 (2006) 1925.
- [15] K.H. Thompson, J. Lichter, C. LeBel, M.C. Scaife, J.H. McNeill, C. Orvig, *J. Inorg. Biochem.* 103 (2009) 554.
- [16] P. Caravan, L. Gelmini, N. Glover, E.G. Herring, H. Li, J.H. McNeill, S.J. Retig, I.A. Setyawati, E. Shuter, Y. Sun, A.S. Tracey, V.G. Yuen, C. Orvig, *J. Am. Chem. Soc.* 117 (1995) 12759.
- [17] T. Kiss, T. Jakusch, D. Hollender, A. Dörnyei, E.A. Enyedy, J. Costa Pessoa, H. Sakurai, A. Sanz-Medel, *Coord. Chem. Rev.* 252 (2008) 1153.
- [18] K. Zborowski, R. Grybos, L.M. Proniewicz, *Inorg. Chem. Commun.* 8 (2005) 76.
- [19] K. Zborowski, R. Grybos, L.M. Proniewicz, *Vibrat. Spectrosc.* 43 (2007) 344.
- [20] J. Seixas de Melo, G. Quinteiro, J. Pina, S. Breda, R. Fausto, *J. Mol. Struct.* 565–566 (2001) 59.
- [21] R. Fausto, G. Quinteiro, S. Breda, *J. Mol. Struct.* 598 (2001) 287.
- [22] D. Lin-Vien, N.B. Colthup, W.G. Fateley, J.G. Grasselli, *The Handbook of Infrared and Raman Characteristic Frequencies of Organic Molecules*, Academic Press, Boston, 1991.
- [23] B. Smith, *Infrared Spectral Interpretation*, CRC Press, Boca Raton, 1999.
- [24] J. Selbin, *Chem. Rev.* 65 (1965) 153.
- [25] E.J. Baran, *J. Coord. Chem.* 34 (2001) 215.
- [26] M. Melchior, S.J. Rettig, B.D. Liboiron, K.H. Thompson, V.G. Yuen, J.H. McNeill, C. Orvig, *Inorg. Chem.* 40 (2001) 4686.
- [27] K.H. Thompson, J. Chiles, V.G. Yuen, J. Tse, J.H. McNeill, C. Orvig, *J. Inorg. Biochem.* 98 (2004) 683.
- [28] K.H. Thompson, C.A. Barta, C. Orvig, *Chem. Soc. Rev.* 35 (2006) 545.
- [29] S.A. Mukha, I.A. Antipova, S.A. Medvedeva, V.V. Saraev, L.I. Larina, A.V. Tsyrenzhapov, B.G. Sukhov, *Chem. Sust. Dev.* 15 (2007) 448.
- [30] J.L. Lamboy, A. Pasquale, A.L. Rheingold, E. Meléndez, *Inorg. Chim. Acta* 360 (2007) 2115.