

Molecular structures of oxovanadium(IV) complexes with maltol and kojic acid: a quantum mechanical study

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Abstract

Molecular structures of two complexes with antidiabetic properties, namely bis(maltolato)oxovanadium(IV) and bis(kojato)oxovanadium(IV), were investigated using quantum chemical methods. All possible structures of the studied compounds were taken into consideration. Our calculation confirmed that the studied compounds formed a pyramidal structure with the vanadyl oxygen on the top, and four ligand's oxygens at the base. Maltolato or kojato units were placed in the *trans* position. A comparison of the obtained theoretical geometries with available experimental data is presented.

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Vanadium compounds show interesting biochemical and pharmacological properties [1]. Intensive studies carried out over the last two decades [2] showed that vanadium is one of the most important supplements for oral diabetes therapy [3]. Inorganic vanadium salts are poorly absorbed from the digestive system, thus high oral doses are required. Therefore, various vanadium ions – organic ligand complexes were tested in order to obtain more potent medicines than inorganic vanadium salts [4].

Several vanadium complexes have been proposed as insulin mimetics [5,6]. Among them oxovanadium(IV) complexes with deprotonated hydroxypyrones, like maltol (3-hydroxy-2-methyl-4H-pyran-4-one, Hma) or kojic acid (5-hydroxy-2(hydroxymethyl)-4H-pyran-4-one, H₂ka) as ligands have been the most promising. The molecular structures of bis(maltolato)oxovanadium(IV)

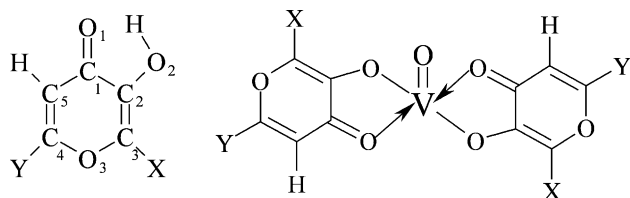
(VO(ma)₂) and bis(kojato)oxovanadium(IV) (VO(H-ka)₂) together with maltol and kojic acid are presented in Fig. 1.

Quantum mechanical calculations have been established for years as proper tools for the determination of the chemical compounds structures. In this work, we examine various structures of VO(ma)₂ and VO(H-ka)₂. The hybrid DFT functional B3LYP [7] combined with the LANL2DZ basis set [8,9], especially dedicated for metal complexes, has been used in this research. Calculations have been executed using the GAUSSIAN98 quantum mechanical package [10]. Geometries of all possible isomers of the studied compounds have been optimized. The calculations of vibrational frequencies have also been performed in order to determine whether the obtained structures constitute minima or saddle points. The complexes under investigation belonged to the open-shielded compounds and had one unpaired electron.

Two kinds of the *cis–trans* isomerism are possible in the studied oxovanadium(IV)–maltol complex. These

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X = CH₃, Y = H - maltol

X = H, Y = CH₂OH - kojic acid

Fig. 1. Structures of the studied compounds.

structures are depicted in Fig. 2. First of all, the whole maltolato units can be placed in the *trans* (structures A and B) or *cis* (structures C and D) positions. Additionally, the maltolato units are placed in such a way that their –CH₃ groups are positioned in the *cis* (structures B and D) or *trans* (structures A and C) manner. Analogical structures are tested in the case of the oxovanadium(IV) complex with kojic acid. The crystal structure of the VO(ma)₂ complex has been already determined [11]. Thus, bis(maltolato)oxovanadium(IV) exists in the *trans–trans* structure (see Fig. 2, structure A). Experimental geometry has been used as the starting point in the *trans–trans* VO(ma)₂ structure calculation. The other structures have been generated by the MOL-DEN program [12].

During geometry optimization, the *cis–cis* and *cis–trans* structures of the VO(ma)₂ transform easily into their *trans–cis* and *trans–trans* counterparts, respectively, exhibiting that they are completely unstable. They can exist only in solutions [13] when a solvent molecule can coordinate to the metal ion and stabilize these structures. The values of total energies for the best *trans–trans* and *trans–cis* geometries of VO(ma)₂ are collected in Table 1. Not all of the structures presented are minima on the potential energy surfaces. That is why the

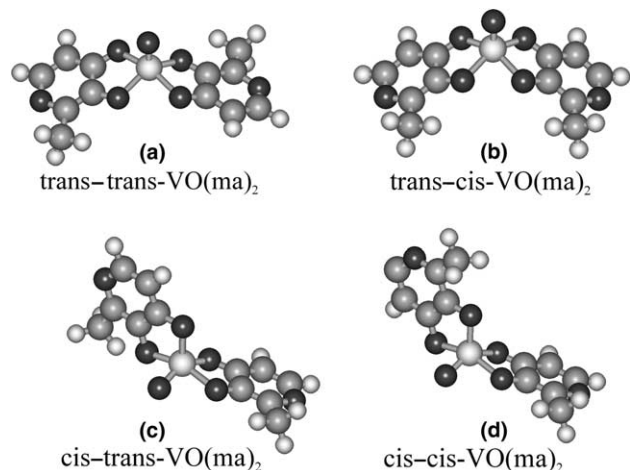


Fig. 2. Different arrangements of maltolato units in VO(ma)₂.

Table 1
Relative energies (kJ/mol) of isomers of the studied oxovanadium(IV) complexes

| Structure | Energy |
|--|--------------------|
| <i>trans–trans</i> -VO(ma) ₂ | 0.00 |
| <i>trans–cis</i> -VO(ma) ₂ | 24.56 ^a |
| <i>trans–trans</i> -VO(Hka) ₂ | 0.00 |
| <i>trans–cis</i> -VO(Hka) ₂ | 13.10 |

Calculations executed at the B3LYP/LANL2DZ level.

^a Saddle point.

zero point energy corrections are not included. The structure with the methyl groups in the *trans* position (*trans–trans* structure) has lower energy than the *trans–cis* one. Additionally, the *trans–cis* structures of VO(ma)₂ predicted by the B3LYP method is the saddle points on the potential energy surface. The calculated geometries as well as the experimental data suggest that the *trans–trans*-VO(ma)₂ structure can belong to the C₂ point symmetry group. In order to check this, we calculated a hypothetical structure having this symmetry. Performed calculations showed that such a structure is not stable (saddle point with one imaginary frequency).

The same calculations have been performed for the bis(kojato)oxovanadium(IV) complex. In addition, conformational analysis has been applied to the –CH₂OH substituent in the kojic acid molecule. The lowest energy has been obtained for the conformation with the torsion angle O(ring)–C(ring)–C(CH₂OH)–O(CH₂OH) close to 180°. Only *trans–trans* and *trans–cis* configurations of the kojato units have been examined. Again, the *trans–trans* structure was more stable than the *trans–cis* one (see Table 1). Here, the energy gap between these two structures was lower than for the VO(ma)₂. The theoretical structure of the oxovanadium(IV)–kojic acid complex is shown in Fig. 3.

A comparison of the experimental [11] and theoretical bond lengths of the studied complexes are gathered in Table 2. The comparison reveals that B3LYP calculation describe the geometry of the oxovanadium(IV)–maltol complex with good quality. The biggest discrepancies were observed for the C₁–C₂ and C₄–C₅ bonds (see Table 2) and they were due to the fact that the comparison is made between the experimental data, obtained from single crystals, and bond lengths calculated for isolated molecules. It has to be pointed out that the obtained geometrical

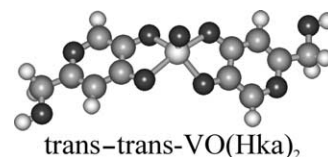


Fig. 3. Suggested structure of the VO(Hka)₂ complex.

Table 2
Selected bond lengths (B3LYP/LANL2DZ, angstrom) for optimal structures of studied compounds

| Bond | Experiment [11] | | <i>trans-trans</i> -VO(ma) ₂ | Δx | | <i>trans-trans</i> -VO(Hka) ₂ |
|--------------------------------|-----------------|-------|---|------------|--------|--|
| | | | Theory | | | Theory |
| O ₁ –C ₁ | 1.281 | 1.266 | 1.303 | –0.022 | –0.037 | 1.301 |
| C ₁ –C ₂ | 1.394 | 1.428 | 1.458 | –0.064 | –0.030 | 1.467 |
| C ₂ –O ₂ | 1.354 | 1.361 | 1.349 | 0.005 | 0.012 | 1.345 |
| C ₂ –C ₃ | 1.407 | 1.336 | 1.383 | 0.024 | –0.047 | 1.375 |
| C ₃ –O ₃ | 1.370 | 1.357 | 1.399 | –0.029 | –0.042 | 1.395 |
| O ₃ –C ₄ | 1.345 | 1.351 | 1.368 | –0.023 | –0.017 | 1.372 |
| C ₄ –C ₅ | 1.306 | 1.297 | 1.373 | –0.067 | –0.076 | 1.375 |
| C ₅ –C ₁ | 1.454 | 1.407 | 1.431 | 0.023 | –0.024 | 1.428 |
| V–O(vanadyl) | 1.596 | | 1.596 | 0.000 | | 1.596 |
| V–O ₁ | 1.999 | 2.022 | 2.050 | –0.051 | –0.028 | 2.052 |
| V–O ₂ | 1.970 | 1.957 | 1.957 | 0.013 | 0.00 | 1.956 |

Δx = experimental bond length – calculated bond length.

For atom numbering scheme, see Fig. 1.

parameters for VO(Hka)₂ are very similar to those predicted for VO(ma)₂.

According to the theoretical results presented in this work, bis(maltolato)oxovanadium(IV) and bis(kojato)oxovanadium(IV) form a pyramidal structure with the vanadyl oxygen on the top, and four ligand's oxygens at the base. The –CH₃ or –CH₂OH substituents take the *trans* position. The *cis* arrangement of the substituents in the pyran ring has always higher energy.

A comparison of the obtained theoretical geometries with the available experimental data was made. The theoretical configurations confirm the published experimental geometry of the oxovanadium(IV)–maltol complex [11]. The obtained results describe the geometry of the studied compounds quite well with only few discrepancies for two C–C bonds in the heterocyclic ring.

The theoretical geometries presented here, will be very useful in the calculations for the compound structures in solution. In that case, the solvent molecule will coordinate in the sixth position to the vanadium ion, forcing efficient *cis-trans* isomerism of the whole deprotonated ligand units.

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