SYNTHESIS AND CHARACTERIZATION OF Zn(II) COMPLEX WITH THE ACETATE AND OROTIC ACID MIX LIGANDS

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ABSTRACT

Semi-empirical calculations were used to characterize the orotic acid structure. The structures optimised using the PM3, AM1, and CNDO methods were compared with the crystallographic data.

Orotic acid is a polydentate ligand due to the net charge on the atoms from the functional group.

A compound was synthesized by reacting orotic acid with zinc acetate dihydrated in a neutral and non-aqueous medium. This compound was characterized by elemental analysis, spectroscopy, and thermal analysis.

The orotic acid replaces water molecules from zinc acetate dihydrate and coordinates through an exo-cyclic oxygen. Based on the probable structure, PM3 semi-empirical calculations of the complex of Zn(II) were performed. The semi-empirical calculations suggest that the orotic acid coordinated through C=O group, where acetate groups maintained the bidentate coordination and the Zn-H₂O distance is greater than that the Zn-H₂O distance for the Zn(II) acetate dihydrate.

Key words: Zinc(II) acetate, metal acetate, orotic acid, semi-empirical calculations.

INTRODUCTION

Orotic acid (Bitamine B₁₂) and its salts play an important role in biological systems as precursors of pyrimidine nucleosides; they are also found in cells and body fluids of many living organisms. These compounds are applied in medicine as biostimulators of the ionic exchange processes in organisms, and different metal complexes of orotic acid have been studied.

Takusagawa and Shimada determined the structure of orotic acid, and other authors have calculated its structure using ab initio methods and by analyzing the vibrational spectra. Orotic acid is a mixture of tautomers, although its crystalline structure in solid state is in a keto form. In the crystal, the molecules are bound by intermolecular forces, such as O–H–N and O=H–O.

Due to its biological importance, the coordination chemistry of orotic acid has been widely studied. It is a multidentate ligand since it can only coordinate through the carboxylic acid group, pyrimidine nitrogen, and exocyclic oxygen (see Figure 1). Metallic orotates of palladium, platinum, and nickel have been synthesized to obtain compounds with possible anticancer activity. T. Solin et al. reacted cis-diamine platinum(II), known for its anticancer properties, with orotic acid, obtaining a compound where the orotic acid coordinates to metal ion through N(1) from the pyrimidine ring and O(4) coming from carboxylic acid group forming a 5-member ring.

Monomer complexes of orotic acid in neutral medium with Co(II), Ni(II), and Cu(II) have been reported, where orotic acid coordinates through an exocyclic oxygen. Zinc(II), dehydrated zinc, is used in medicine to treat the Zn(II) deficiency in organisms.

Based on the probable structure, PM3 semi-empirical calculations of Zn(acetate)·2H₂O, the Zn-O acetate groups coordinated to the metal ion through a bidentate coordination show a high percentage of ionic character.

There is great interest to synthesize model complexes of zinc containing enzymes. Consequently, complexes containing other N- donor ligands have been prepared, and complexes with monomer ligands and polymer ligands with functional groups containing nitrogen have been studied.

Ligands can coordinate with zinc(II) acetate dihydrate, replacing the water molecules and keeping the bidentate coordination of the acetate groups. In the case of the imidazole ligand, the complex Zn(him)(MeCO₂), has been reported where the acetate groups are coordinated in a monodentate manner.

The aim of this article is to carry out semi-empirical calculations for orotic acid with zinc(II) dihydrate acetate in a neutral medium to obtain a compound with mix ligands.

EXPERIMENTAL

Materials: Zn(CH₂COO)₂·2H₂O p.a (Merck), orotic acid (Aldrich) were used without further purification.

Preparation of complex: Finely powder samples of orotic acid monohydrate and zinc acetate dihydrate were mixed in 2:1 stoichiometric quantities and ethyl acetate (250 mL) was added. After boiling under reflux for 40 h., a precipitate was obtained, which was filtered, washed with ethyl acetate, and dried at 60 °C up to constant weight. The precipitate is insoluble in polar and non-polar solvents.

(Found: Zn: 12.0 %  N: 11.5 %, Calcd.: Zn 13.4 %, N: 11.5%).

Measurements: Elemental analyses of nitrogen were obtained using a Series II CHNS 10 analyzer 2400 Perkin Elmer. Zn(II) was analyzed by atomic absorption spectrometry with a Perkin Elmer model 3100. The FT IR spectra of the samples were recorded on a Magna Nicolet 550 and a Nicolet Nexus spectrophotometers. Thermogravimetric analyses of the polychelates were performed with a Polymer Laboratories STA 625 analyzer.

Quantum Chemical Calculations: AM1, CNDO and PM3 semi-empirical calculations were carried out using a MOPAC program that is included in HyperChem 7. The compounds were created graphically with support of the HyperChem Program. It was optimized by molecular mechanical and subsequently by PM3 calculation method.

RESULTS AND DISCUSSION

By comparing the crystalline structure of monohydrated orotic acid reported by Takusagawa and Shimada with the semi-empirical calculations, an important difference in the bond length of the exocyclic bonds C=O is observed (see Table 1, figure 1).

In the crystalline structure, the bond C(2)-O(1) has a length of 1.227 Å and the bond C(4)-O(2) has a higher value 1.230 Å. However, according to the semi-empirical calculations AM1 and PM3, from anhydrous orotic acid the bond C(4)-O(2) is shorter than the C(2)-O(1) bond and the atom O(1) presents a higher net charge. In the structure of thymine, the bond C(4)-O(2) (1.230 Å) is slightly shorter than the bond C(2)-O(1) (1.234 Å). The CNDO-reported calculations show the highest net charge on the atom O(1). CNDO calculations of the orotic acid structure were performed and the bond C(2)-O(1) is slightly lower than the bond C(4)-O(2). The net charge on the atoms of functional groups, calculated with the CNDO, AM1, and PM3 methods, demonstrate that the O(1) bound to C(2) is the one with the higher net charge (see Table 2).

The bond length for C=O and the functional group that presents the higher charge density are needed to explain the vibrational spectrum as well as the exocyclic C=O coordination with the metal.
Orotic acid, by reacting with Zn(acetate)$_2$·2H$_2$O, removes two water molecules and coordinates with the meta ion. The thermogravimetric analysis shows the loss of acetate between 200-320 ºC and the loss of orotic acid between 325-400 ºC (see Table 3 and Figure 2).

Table 2. Net charge on some selected atoms.

<table>
<thead>
<tr>
<th>Atom (No)</th>
<th>CNDO</th>
<th>AM1</th>
<th>PM3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N(1)</td>
<td>-0.182</td>
<td>-0.325</td>
<td>-0.081</td>
</tr>
<tr>
<td>C(2)</td>
<td>0.427</td>
<td>0.404</td>
<td>0.219</td>
</tr>
<tr>
<td>N(3)</td>
<td>-0.209</td>
<td>-0.361</td>
<td>-0.004</td>
</tr>
<tr>
<td>C(4)</td>
<td>0.346</td>
<td>0.344</td>
<td>0.283</td>
</tr>
<tr>
<td>C(5)</td>
<td>-0.098</td>
<td>-0.203</td>
<td>-0.173</td>
</tr>
<tr>
<td>C(6)</td>
<td>0.125</td>
<td>0.019</td>
<td>-0.128</td>
</tr>
<tr>
<td>C(7)</td>
<td>0.347</td>
<td>0.332</td>
<td>0.394</td>
</tr>
<tr>
<td>O(1)</td>
<td>-0.388</td>
<td>-0.348</td>
<td>-0.374</td>
</tr>
<tr>
<td>O(2)</td>
<td>-0.341</td>
<td>-0.304</td>
<td>-0.328</td>
</tr>
<tr>
<td>O(3)</td>
<td>-0.271</td>
<td>-0.259</td>
<td>-0.298</td>
</tr>
<tr>
<td>O(4)</td>
<td>-0.229</td>
<td>-0.267</td>
<td>-0.252</td>
</tr>
</tbody>
</table>

Orotic acid has been reported to coordinate with the oxygen of group $\text{C}=\text{O}$, and the absorption band at 1660 cm$^{-1}$ is assigned to the $\text{C}=\text{O}$ stretching of the carboxyl group. The band at 1739 cm$^{-1}$ observed for orotic acid is split in absorption bands at 1728 and 1715 cm$^{-1}$, which is assigned to the $\text{C}=\text{O}$ stretching vibration of the carboxyl group coupled with stretching of $\text{C}=$ from the ring.

The FT-IR of compound Zn(acetate)$_2$·2H$_2$O shows the following absorption bands: at 2500 cm$^{-1}$ stretching of $\text{OH}$ (COOH), at 1700 cm$^{-1}$ stretching of $\text{C}=\text{O}$ (COOH) coupled with stretching band of $\text{C}=$ from the ring.

The following reaction is suggested: $\text{Zn(CH}_3\text{COO)}_2\cdot\text{2H}_2\text{O} + 2\text{H}_2\text{O} \rightarrow \text{Zn(CH}_3\text{COO)}_2\cdot\text{2H}_2\text{O}$. Orotic acid has been reported to coordinate with the oxygen of group $\text{C}(4)-\text{O}(2)$ in neutral medium.

Maistralis et al. have assigned different bands to the IR spectrum: at 2500 cm$^{-1}$ stretching of $\text{OH}$ (COOH), at 1700 cm$^{-1}$ stretching of $\text{C}=\text{O}$ (COOH) coupled with stretching band of $\text{C}=$ from the ring.

The FT-IR of compound Zn(acetate)$_2$·2H$_2$O shows the following absorption bands: at 2500 cm$^{-1}$ stretching of $\text{OH}$ (COOH), due to intermolecular interactions of carboxylic acids, which corroborates that this group is not participating in the coordination. The orotic acid absorption bands at 1700 and 1660 cm$^{-1}$ are shifted to 1715 and 1648 cm$^{-1}$.

To deconvolute the FT IR spectra in the $\text{C}=\text{O}$ absorption region of the orotic acid and the compound, the absorption band observed at 1700 cm$^{-1}$ is split in two bands. The band of orotic acid is split in absorption bands at 1739 and 1699 cm$^{-1}$, and the Zn complex is split in bands at 1728 and 1715 cm$^{-1}$.
acetate groups. The latter shows a slightly lower $\nu$ $H\_2O$ and for a structure with monodentate acetate groups. The former calculations were performed considering a structure with the bidentate calculated using the semi-empirical PM3 method (see Figure 3 and Table 5).

An unsymmetric stretching band of $COO^-$ appears at 1620 cm$^{-1}$, but the symmetric stretching vibration can be not assigned since the orotic acid presents several absorption bands in this region.

Table 4 Calculations of some stretching vibrations of $H\_2O$ and Zn(CH$_3$COO)$_2$($H\_2O$)$_n$.

<table>
<thead>
<tr>
<th>$\nu$ (cm$^{-1}$)</th>
<th>H$_2$O</th>
<th>Zn(CH$_3$COO)$_2$($H_2O$)$_n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\nu$ (C=O).</td>
<td>1739</td>
<td>1978</td>
</tr>
<tr>
<td>$\nu$ (C=O).</td>
<td>1699</td>
<td>1938</td>
</tr>
<tr>
<td>$\nu$ (C=O).</td>
<td>1660</td>
<td>1897</td>
</tr>
</tbody>
</table>

PM3 calculations have not been corrected.

Coordination appears to occur through an oxygen from C$_1$:O since the semi-empirical calculations show higher electronic density and the stretching absorption band corresponding to C$_2$:O is significantly shifted from 1660 to 1648 cm$^{-1}$.

The Zn-OH$_2$ stretching vibration in the IR far spectrum of Zn(CH$_3$COO)$_2$H$_2$O· is observed at 394 cm$^{-1}$, but this band is not observed in the complex’s spectrum, corroborating that the water molecules were removed by the orotic acid. In the region of Zn-O vibrations, two bands at 280 and 185 cm$^{-1}$ are observed.

According to the experimental data, the complex’s structure was calculated using the semi-empirical PM3 method (see Figure 3 and Table 5). The calculations were performed considering a structure with the bidentate acetate groups and for a structure with monodentate acetate groups. The former shows a slightly lower $\Delta H_{formant}$ suggesting a structure with the two bidentate acetate groups.

\[\text{Table 5. Selected PM3 structural parameters of Zn(CH$_3$COO)$_2$· 2H$_2$O, H$_2$O, and Zn(CH$_3$COO)$_2$($H\_2O$)$_2$.}\]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Zn(CH$_3$COO)$_2$($H_2O$)$_2$</th>
<th>Zn(CH$_3$COO)$_2$· 2H$_2$O</th>
<th>H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bond length ($\AA$)</td>
<td>Zn(1)-O(2)</td>
<td>1.986</td>
<td>2.075</td>
</tr>
<tr>
<td></td>
<td>Zn(1)-O(3)</td>
<td>2.762</td>
<td>2.783</td>
</tr>
<tr>
<td></td>
<td>Zn(1)-O(31)</td>
<td>3.235</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zn(1)-O(9)</td>
<td>2.327</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C(32)-O(31)</td>
<td>1.252</td>
<td>1.223</td>
</tr>
<tr>
<td></td>
<td>C(34)-O(38)</td>
<td>1.216</td>
<td>1.218</td>
</tr>
<tr>
<td></td>
<td>Zn-OF$_2$</td>
<td>2.209</td>
<td></td>
</tr>
</tbody>
</table>

The structural parameters of the complex Zn(CH$_3$COO)$_2$($H\_2O$)$_2$ does not show important differences with the parameters of Zn(CH$_3$COO)$_2$· 2H$_2$O and H$_2$O without coordination. The greatest difference is observed for the distance between Zn and the oxygen of the orotic acid, which is greater than the distance of Zn-OH$_2$ in Zn-acetate dihydrate. Nevertheless, the oxygen from orotic acid, which coordinates to metal ion, has a higher charge density than the oxygen of water. This result can be explained by the higher size of H$_2$O. On the other hand, there are important changes in the distribution charges with a higher electronic delocalization.

CONCLUSIONS

Orotic acid in neutral medium is coordinated through exocyclic C=O to coordinate with Zn(II) in Zn(CH$_3$COO)$_2$· 2H$_2$O by replacing water-molecules. The semi-empirical calculations suggest that the orotic acid coordinated through C$_1$:O group, where acetate groups maintained the bidentate coordination and the Zn- H$_2$O distance is higher than that the Zn- H$_2$O distance for the Zn(II) acetate dihydrate.

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REFERENCES


Fig. 3. PM3 structure of Zn(CH$_3$COO)$_2$($H\_2O$)$_2$.\[\text{J. Chil. Chem. Soc., 55, Nº 1 (2010)}\]