Divalent transition metal complexes of the anionic form of 4,7-dihydro-1,2,4-triazolo[1,5-a]pyrimidine-7-one: crystal structure of the zinc(II) compound

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Abstract

Several complexes of the ligand 4,7-dihydro-1,2,4-triazolo[1,5-a]pyrimidine-7-one (7HtpO) in its anionic form (7tpO−) with divalent metals (the complete first series from Mn to Zn plus Cd) have been synthesized and characterized by means of analytical techniques (elemental analysis, thermogravimetry and differential scanning calorimetry), spectral methods (IR and electronic spectroscopy), magnetic measurements (77–290 K) and EPR in the case of the Cu compound. All compounds display a M(7tpO)2nH2O stoichiometry. The crystal structure of [Zn(7tpO)2(H2O)4]. 2H2O has been solved by single crystal X-ray diffraction. In this compound, the ligand 7tpO− binds the metal ion through the N atom in position 3 and four water molecules complete the slightly distorted octahedral environment with the Zn atom occupying an inversion center. For all other compounds except Cu, infrared data suggest that the ligand binds in a similar fashion whereas visible spectroscopy and magnetic measurements point to octahedral geometry. On the other hand, magnetic and EPR measurements of the copper compound indicate that it is dinuclear with an antiferromagnetic coupling constant 2J = −87.8 cm−1 and a zero-field splitting parameter D = 0.168 cm−1.

Keywords: Triazolopyrimidine; Zn complexes; Copper dimers; EPR

1. Introduction

The 1,2,4-triazolo[1,5-a]pyrimidine ring has a chemical structure similar to purine, differing from it by the presence of a pyrimidine nitrogen atom in a bridgehead position with the disappearance of the acidic H-proton of the five-membered ring [1]. Metal complexes of these heterocycles may be considered as model systems for some naturally occurring metal coordination compounds. The study of the interaction of metal cations with 1,2,4-triazolo[1,5-a]pyrimidine derivatives has been carried out by a few research groups including one at the State University of Leiden [2] and more recently another one at the Nicholas Copernicus University at Torun [3], apart from our group at the University of Granada. The work in this field previous to 1999 was reviewed by us [4].

Single crystal X-ray diffraction studies of these metal complexes display an appreciable variability in their molecular structures. There are examples of mononuclear compounds, usually with the ligand monodentately bound through the nitrogen atom at position 3 [5], but with a few cases showing chelating behaviour through an endocyclic N atom and an exocyclic O atom [6]. There are also many examples of binuclear or polynuclear compounds in which the metal atoms are bridged either by the triazolopyrimidine derivative [7] or by other auxiliary ligands [8]. The biological activity of a number of these complexes have been tested, finding that some of them inhibit the growth of Gram(+) and Gram(−) bacteria [9,10] as well as other parasites [11]. Antitumour activity has also been detected for several platinum group metals with triazolo[1,5-a]pyrimidine derivatives [12].
Most of the work in this field has been mainly focused on a few metal ions, namely platinum group metals [13], silver(I) [14] and copper(II) [15] with few examples of other divalent cations [16]. Following this research line, we present in this paper the synthesis, spectroscopic characterization, thermal and magnetic behaviour of a series of divalent metal complexes (Mn to Zn plus Cd) bearing the anionic form of 4,7-dihydro-1,2,4-triazolo[1,5-a]pyrimidine-7-one (7HtpO), which is an isomer and mimic of the purine base hypoxanthine. The crystal structure of the zinc compound is described. The molecular structure of the ligand and the numbering scheme for its atoms are shown in Scheme 1.

2. Experimental

2.1. Synthesis of the complexes

The compound 4,7-dihydro-1,2,4-triazolo[1,5-a]pyrimidine-7-one (7HtpO) was prepared according to published method from 3-amino-1,2,4-triazole and malic acid in strong acidic medium [17]. Other reagents were obtained from commercial sources.

Metal complexes were obtained by mixing two aqueous solutions, 10 mL each, one containing 0.1 g of 7HtpO and the other containing 0.1 g of the appropriate salt (sulfate for Mn and Fe, and acetate for Ni, Co, Cu, Zn and Cd). A small pH adjustment was necessary in the case of Mn and Ni, five drops of 1 M NaOH were added in the first case and one drop of concentrated acetic acid was added in the second. From the solution containing 7HtpO and zinc acetate, colorless crystals of the complex suitable for X-ray analysis were isolated after 24 h. The other complexes were obtained as powders from their corresponding solution after 24 h except for Cd for which the compound precipitated immediately. In all cases, the solids were washed with water and ethanol and dried with ether.

From elemental analyses, the following formulae were deduced for the isolated compounds:


2.2. Instrumentation

Microanalysis of C, H and N were performed in a Fisons Instruments EA-1008 analyzer. Thermal behaviour was studied under an air flow in Shimadzu TGA-50 and Shimadzu DSC-50 equipment. Reflectance diffuse spectra were recorded in a Cary-5 spectrophotometer. Magnetic susceptibility was measured in a Manics DSM-8 Faraday balance. An electron paramagnetic resonance spectrum was obtained in a X-band Bruker ESP-300E apparatus (all this equipment was sited at the Centre of Scientific Instrumentation of the University of Granada). IR spectra were obtained using a FT MIDAC Prospect 1 spectrophotometer with samples dispersed in KBr pellets.

2.3. Crystallography

Data were collected at room temperature for a brick-shaped colourless crystal (dimensions 0.20 x 0.24 x 0.32 mm) in a Stoe Stadi4 diffractometer with Mo Kα radiation (λ = 0.7107 Å). Data were corrected for absorption (ψ-scans, transmission range, 0.6309–0.7119). The structure was solved by the heavy atom method and refined in F2 using SHELXL-97 [18]. Hydrogen atoms of the heterocycle were placed in ideal positions and those of water molecules were located and refined with fixed (0.86 Å) O–H distances. Isotropic thermal parameters of all H atoms were fixed to 1.2 times the equivalent isotropic thermal parameter of their parent atoms.

Crystal data for [Zn(C6H4N3O)2(H2O)4]·2H2O, orthorhombic, space group Pcca, a = 7.5430(8), b = 13.1384(12), c = 17.2599(10) Å, V = 1710.5(3) Å3, Z = 4, Dcalc = 1.723 Mg m–3, μ = 1.497 mm–1, 2487 unique reflections collected (θ range, 2.36°–30°), wR2 = 0.2760, R (for 1389 data with I > 2σ(I)) = 0.0872.
3. Results and discussion

3.1. X-ray structural study of the zinc compound

Fig. 1 displays the molecular structure of compound 6. The crystal structure comprises separate molecules of [Zn(7tpO₂(H₂O)₄)] in which the metal atom lies in a crystallographic inversion center. Its environment is a slightly distorted octahedron defined by two symmetry related 7tpO⁻ ligands in trans disposition, and four water molecules. The two 7tpO⁻ ligands are coordinated in a monodentate manner through the N atom in position 3, which is the most frequent binding site for this type of ligand [4] This behaviour is also found in the analogous 5-methylated derivative, although an example of N1-O7 chelation has also been described for this compound with copper [15] as well as for the 5,7-dioxo analogues of octahedral species [21]. Thus, the spectrum of 2 shows two overlapped bands even if only one is expected for a high spin configuration, which can be due to a strong Jahn–Teller distortion of the excited state. The splitting energy between the 2g and 3g levels has been calculated as the average of the two bands, the corresponding value being Δo = 10160 cm⁻¹. The cobalt complex 3 exhibits a spectrum with two main absorptions: a broad one centered at 8420 cm⁻¹, assigned to the 4T₂g(F) ← 4T₁g(F) (ν₁) transition and another at 20325 cm⁻¹, assigned to 4T₁g(P) ← 4T₂g(P) (ν₂). This band presents a shoulder at higher wavenumber that could be

Zn(H₂O)₄ plane (dihedral angle 93.5(2)°) and the projection of the first plane over the second bisects the O1W-Zn-O2W angle (torsion angle C3a-N3-Zn-O1W, -44.3(5)°) which minimizes steric repulsions.

All hydrogen atoms of both coordinated and non-coordinated water molecules are involved in hydrogen bonds stabilizing the structure (see Table 1). The main acceptor of these bonds is the exocyclic oxygen atom of 7tpO⁻.

3.2. Spectral, thermal, magnetic and EPR studies

The thermal study of these compounds in air has been carried out from their TG and DSC plots. All compounds are hydrated and loss of water is the first step of their thermal decomposition. For compound 5 (Cu), the corresponding effects are very broad showing the unspecific nature of water, the percentage of which is not reproducible. The remaining complexes display well defined weight losses in the range 50–180 °C which agree well with the number of water molecules indicated by their elemental analysis. Dehydration takes place in a single step (endothermic peaks in the range 98–110 °C) except for 4 (Ni) for which two well-defined stages are observed (peaks at 92.2 and 121.4 °C). Dehydration energy is very similar for all the compounds, ranging from 45.5 to 48.8 kJ/mol of water. The anhydrous complexes are stable up to ~350 °C, when pyrolytic decomposition starts.

The infrared spectra of the complexes 1–4, 6 and 7 are virtually identical, differing from that of the free ligand [17] by the presence of a broad band at 3400 cm⁻¹ due to ν(O–H) of water molecules, the absence of the intense ν(N–H) band and the bathochromic shift of ν(C=O) which appears at 1625–1630 cm⁻¹. On the other hand, the spectrum of 5 (Cu) is noticeably different from the other: thus, the bathochromic shift of ν(C=O) vibration is smaller (band at 1674 cm⁻¹), which may indicate a different coordination mode of the ligand. Such different behaviour of copper(II) if compared with the rest of the divalent transition ions has also been observed for the complexes of the analogous ligand that contains a second oxygen atom at position 5 [6].

The diffuse reflectance spectra of 2, 3 and 4 are typical of octahedral species [21]. Thus, the spectrum of 2 shows two overlapped bands even if only one is expected for a high spin configuration, which can be due to a strong Jahn–Teller distortion of the excited state. The splitting energy between the 2g and 3g levels has been calculated as the average of the two bands, the corresponding value being Δg = 10160 cm⁻¹. The cobalt complex 3 exhibits a spectrum with two main absorptions: a broad one centered at 8420 cm⁻¹, assigned to the 4T₂g(F) ← 4T₁g(F) (ν₁) transition and another at 20325 cm⁻¹, assigned to 4T₁g(P) ← 4T₂g(P) (ν₂). This band presents a shoulder at higher wavenumber that could be

![Fig. 1. Molecular structure of compound 6 as deduced from X-ray diffraction data. Nonhydrogen atoms are represented by ellipsoids at the 50% probability level.](image-url)

Table 1

<table>
<thead>
<tr>
<th>Coordination sphere</th>
<th>Selected interatomic distances (Å) and angles (°)</th>
</tr>
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<tbody>
<tr>
<td>Zn–N3 2.125(5)</td>
<td>N3–Zn–O1W 92.0(2)</td>
</tr>
<tr>
<td>Zn–O1W 2.113(4)</td>
<td>N3–Zn–O2W 89.4(2)</td>
</tr>
<tr>
<td>Zn–O2W 2.143(5)</td>
<td>O1W–Zn–O2W 89.3(2)</td>
</tr>
<tr>
<td><strong>Hydrogen bonds</strong></td>
<td></td>
</tr>
<tr>
<td>O1W···O3W (1/2 + x, 1/2 − y, 1 − z)</td>
<td>2.697(6)</td>
</tr>
<tr>
<td>O1W···O3W (−1/2 + x, 1/2 − y, 1 − z)</td>
<td>2.765(7)</td>
</tr>
<tr>
<td>O2W···O7 (1/2 − x, 1 − y, −1/2 + z)</td>
<td>2.740(6)</td>
</tr>
<tr>
<td>O2W···O7 (−1/2 + x, 3/2 − y, 1 − z)</td>
<td>2.892(6)</td>
</tr>
<tr>
<td>O3W···O4 (1/2 + x, 1/2 − y, 1 − z)</td>
<td>2.791(6)</td>
</tr>
<tr>
<td>O3W···O7 (3/2 + x, 1 − y, −1/2 + z)</td>
<td>2.772(7)</td>
</tr>
</tbody>
</table>
due to the proximity of the 2A_{2g} level or to spin–orbit coupling, which would also be responsible for the asymmetry of the v_{1} band. Ligand field parameters were calculated by Dou equations [22] on the basis of octahedral geometry giving D_{o} = 9580 and B_{o} = 872 cm\(^{-1}\). The transition 4A_{2g}(F) \rightarrow 4T_{1g}(F)(v_{2}) may be assigned to the weak shoulder at 18 000 cm\(^{-1}\). The spectrum of 4 shows the typical three bands expected for octahedral Ni(II) complexes at 9530 (3T_{2g} \rightarrow 3A_{2g}), 15 600 (3T_{1g} \rightarrow 3A_{2g}) and 26 385 cm\(^{-1}\), from which the parameters D_{o} = 9530 cm\(^{-1}\) and B_{o} = 982 cm\(^{-1}\) were calculated. Finally, the spectrum of the copper complex 5 presents a very broad band with a shoulder, with a maximum at 17 150 cm\(^{-1}\) that can be attributed to a d–d transition in a d\(^{9}\) configuration with distorted octahedral geometry (this may include tetragonal pyramidal or square planar). An additional band at 25 100 cm\(^{-1}\) may be attributed to a ligand–metal charge transfer transition.

The magnetic susceptibility of the paramagnetic compounds has been measured as a function of temperature and corrected for diamagnetism [23]. The values for compounds 1–4 have been adjusted by least squares to the Curie–Weiss law yielding the values of \(\theta\) and \(\mu_{\text{eff}} (T \rightarrow \infty)\) indicated in Table 2, which also collects the values of \(\mu_{\text{eff}}\) at 100 and 298 K. These are normal values for octahedral complexes and the variation with T for 2 and 3 (reflected in the negative values of \(\theta\)) is attributable to the orbital contribution in a T ground state.

Compound 5 presents a quite different behaviour, the representation of the magnetic susceptibility versus T in the range 5–300 K shows a maximum at 70 K (Fig. 2), which is indicative of an antiferromagnetic interaction between the copper centers. Data have been fitted to the Bleany–Bowers equation for Cu(II) dimers [24] including the correction due to the presence of a small amount of the mononuclear species (indicated by the points at very low T). From this fitting the following values were obtained: \(g = 2.17, 2J = -87.82\) cm\(^{-1}\), \(\rho = 0.12\).

The X-band EPR spectrum of a powdered sample of this compound at room temperature also suggest its dinuclear nature. The main features of this spectrum have been assigned to (S = 1, \(\Delta M_{S} = 1\)) transitions with axial symmetry. By means of computer simulations with the XEMR program [25], the values \(g_{\parallel} = 2.25, g_{\perp} = 2.00, D = 0.168\) cm\(^{-1}\) have been obtained. Fig. 3 represents the experimental and the simulated spectra. The differences are attributable to the signal of the S = 1/2 transition (mononuclear species, around 3200–3300 G), not included in the simulation and the possible existence of a \(\Delta M_{S} = 2\) (half-field) transition which should overlap with the strong signal at 1300–1500 G.

The magnetic susceptibility and EPR data are very similar to those found for the dimeric copper complex.

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Table 2

<table>
<thead>
<tr>
<th>Compound</th>
<th>(\mu_{\text{eff}}) (100 K)</th>
<th>(\mu_{\text{eff}}) (298 K)</th>
<th>(\mu_{\text{eff}} (T \rightarrow \infty))</th>
<th>(\theta) (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Mn)</td>
<td>6.08</td>
<td>6.03</td>
<td>6.00</td>
<td>+2.6</td>
</tr>
<tr>
<td>2 (Fe)</td>
<td>5.37</td>
<td>5.42</td>
<td>5.42</td>
<td>-1.9</td>
</tr>
<tr>
<td>3 (Co)</td>
<td>4.90</td>
<td>4.98</td>
<td>5.03</td>
<td>-5.1</td>
</tr>
<tr>
<td>4 (Ni)</td>
<td>3.24</td>
<td>3.24</td>
<td>3.24</td>
<td>+1.2</td>
</tr>
</tbody>
</table>

\(\mu_{\text{eff}}\) values are in BM.
with the isomeric ligand 4,5-dihydro-1,2,4-triazolo[1,5-a]pyrimidine-5-one (5HtpO) [26], which let us propose for compound 5 a dinuclear structure with two metal atoms bridged by four 7tpO/C0 moieties linked through the N atoms at positions 3 and 4. Copper(II) complexes of purine bases with this kind of structure and strong antiferromagnetic coupling have been described [27] including one of hypoxanthine [28], the purine base for which 7HtpO is a mimic.

4. Supplementary data

The supplementary crystallographic data for this paper have been deposited in the CCDC (Deposition No. CCDC 220311). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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References