Novel amidrazone derivative and its Cu(II) complex: Crystal structure and antitumor activity

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Compounds with an open chain amidrazone system, \( \text{N} - \text{C} = \text{N} - \text{N} \), (Scheme) constitute a unique group of ligands with their propensity to react with a wide range of transition metals in their neutral or ionic forms as well as diversity of their coordination modes [1]. Depending on the quality of the metal center and experimental conditions they can form mono-, bi- and poly-nuclear species. These properties make them useful in design and synthesis of novel functional materials. However, the most extensive studies of hydrazones are related to their pharmacological properties. It has been shown that some of them exhibit significant antibacterial and antitumor properties [2], [3].

X-ray diffraction analysis of 6-acetyl-cyclohex-3-ene-carboxylic acid [1-pyrindin-2-yl-1-(pyridyn-2-yloamin)meth-(Z)-ylidene] hydrazide, \( \text{H}_2\text{L}_1 \), (1) and its copper(II) complex \([\text{Cu}L_2] \cdot 4\text{H}_2\text{O} \), (2) has been carried out in order to elucidate the influence of coordination and amide protonation state on the geometry of the ligand.

\[
\begin{align*}
\text{H}_2\text{L}_1 (1) & \\
[\text{Cu}L_2] \cdot 4\text{H}_2\text{O} (2) & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{L}_1 (1) & \\
\alpha & = 10.769(2) \text{ Å} \\
b & = 11.423(1) \text{ Å} \\
c & = 14.628(2) \text{ Å} \\
\alpha & = 90.051(1) ^\circ \\
\beta & = 90.041(1) ^\circ \\
\gamma & = 103.39(1) ^\circ \\
V & = 1775.0(4) \text{ Å}^3 \\
Z & = 4 \\
R & = 0.0511 \\
R_w & = 0.0484 \\
\end{align*}
\]

Structural analysis showed that compound (1) exists in its amide-hydrazone form in the solid state. The central amidrazone moiety has a Z configuration with respect to the hydrazone \( \text{C} = \text{N} \) double bond. The \( \text{N} \)\( = \text{C} \)\( = \text{N} \)\( = \text{O} \) chain, which adopts a cis,trans,cis conformation, is almost planar. All atoms of the acylamidrazone moiety may be regarded as sp\(^2\) hybridized. Near-planarity of this unit may suggest a high level of \( \pi \)-electron delocalization. However, the X-ray data indicate, that there is a clear distinction between single and double bonds in this part of molecule.

The reaction of \( \text{H}_2\text{L}_1 \) (1) with copper(II) acetate results in double protonation of the ligand, namely the carboxylic and amide groups. This induces considerable \( \pi \)-electron delocalization along the whole acylamidrazone system. Furthermore, the ligand configuration is found to be transferred from Z to E upon metal complexation. The elementary building units in crystal (2) are centrosymmetric binuclear species. Isomerization around the \( \text{C} = \text{N} \) bond allows the \( \text{L}^2 \) ions to chelate the \( \text{Cu}^{2+} \) ion through its pyridine-N, amide-O and imine- N atoms. The carboxylate O atom from the adjacent, inversion-related ligand completes the square-planar donor arrangement around the metal center.

In cytotoxicity research, (2) shown a high in vitro cytotoxic properties against SW 948, CX-1 and A-431 cancer cell lines, whereas growth inhibition activity of the free ligand (1) was no significant.

This work was supported by the Polish Ministry of Science and Higher Education (project No. N204 346839).

Keywords: amidrazone, copper complex, crystal structure

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