

Structures of Vitamin B₁₃ Complexes with Transition Metal Ions. The Role of Unusual Cu(II)··· π Interaction and Hydrogen Bonds.

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Vitamin B₁₃ (orotic acid, 6-carboxyuracil) is indispensable in biological systems as a key precursor in the biosynthesis of pyrimidine nucleotides of nucleic acids. Recently, this compound has attracted growing attention in medicine as the carrier for certain metal ions. Metal orotates can be used in curing syndromes related with metal ion deficiencies and also as promising therapeutic agents for cancer and heart diseases. Vitamin B₁₃ is also interesting multidentate ligand. The coordination chemistry of orotic acid was investigated in numerous papers, however our studies with single crystal X-ray diffraction, vibrational spectroscopy and quantum chemistry methods have provided new insights into the binding properties of this ligand [1,2].

The recently reported crystal structure of *cis*-[Cu(orotate)(NH₃)₂] has revealed the presence of the unusual Cu²⁺··· π binding force, in this complex [1]. The coordination sphere of the Cu²⁺ ion can be described as a (4+1+1) geometry, where one axial position is occupied by the carbonyl oxygen atom of the neighboring uracil ring, but the other axial site, surprisingly, is located at the C=C double bond of another uracil ring. This is the first case, where the π -type interaction between the chelated Cu²⁺ ion and the C=C bond is clearly demonstrated. Thus far, only the Cu⁺-benzene complex has been detected [3]. In this work, we have explored the nature of this interaction by the spectroscopic and theoretical studies using the *ab initio* second-order Moller-Plesset perturbation (MP2) and density functional (B3LYP) methods with several basis sets. According to our results, the dispersion energy is very important in this non-covalent Cu²⁺··· π binding interaction.

The role of hydrogen bonds has also been investigated. In *cis*-[Pt(orotate)(NH₃)₂], a new cisplatin analogue, strong intramolecular N-H···O hydrogen bond may have significant influence on the biological activity of this compound. In [Ni(H₂O)₆][Horotate]₂·2H₂O, the [Ni(H₂O)₆]²⁺ cation is associated with two trans-related [Horotate]⁻ anions only *via* hydrogen bonds between the oxygen carboxylate atoms and the water molecules coordinated to the metal cation. In all these complexes, the orotate ligands are also engaged in “base-pairing” hydrogen bonds between the planar uracil rings. This indicates that Vitamin B₁₃ can form complementary hydrogen bonds with the adenine residues in many biological molecules, and it may serve as the carrier molecule, which transports metal ions through the cell membranes.

[1] D. Michalska, K. Hernik, R. Wysokiński, B. Morzyk-Ociepa, A. Pietraszko, *Polyhedron* 26 (2007) 4303.

[2] R. Wysokiński, K. Hernik, R. Szostak, D. Michalska, *Chem. Phys.* 333 (2007) 37.

[3] F. Meyer, F.A. Khan, P.B.J. Armentrout, *J. Am. Chem. Soc.* 117 (1995) 9740.