MS36-P12 Effect of methyl and hydroxyl substitution to the single crystal formation of some hydroxypyridinecarboxylic acids and their copper(II)complexes

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A few methyl and hydroxyl substituted hydroxypyridinecarboxylic acids (HPC's) and their copper(II)complexes have been synthetized, crystallized and their structure were investigated by single crystal X-ray diffraction. These compounds are part of a series of HPC compounds which were developed as potential metal chelators for the treatment of metal overload. Redox active metals, like iron and copper, can undergo redox cycling and cause oxidative stress by increasing the formation of reactive oxygen species (ROS), resulting in the damage of many biomolecules in the cells. Copper overload is implicated in the pathogenesis of a variety of human diseases like cancer, cirrhosis, atherogenesis and neurodegenerative diseases, and it plays a key role in the copper metabolism disorders as Menkes and Wilson diseases. Similarly, iron overload is one of the most common metal toxicity diseases worldwide. Chelation therapy aims to remove toxic metal ions from human body or attenuate of their toxicity by transforming them into less toxic compounds. The basic requirement of a chelator is the stability of its complexes, which must be completely formed before their excretion. As the chelators should fulfill specific bio-chemical properties (high complex stability, fast formation kinetics, high selectivity for specified ion, good bioavailability, low toxicity), the design of non-toxic but metal-selective ligands is extremely difficult. Structural information about these ligands and their metal complexes can significantly support the drug developing. As a systematic series of HPC' with slightly altered molecules are investigated, the understanding of the supramolecular interactions (H-bridge, electrostatic coupling and other secondary interactions) exhibited in solid state will facilitate the fine-tuning of the structural properties in order to produce new substances with required properties. Our goal is to investigate the structure of these ligand molecules and their metal complexes (especially with copper(II)) by single crystal X-ray diffraction. The structure of two free ligands (space groups *Pna2*$_1$ and *P2*$_1$*/c*), one of them also as HCl salt (space group *P2*$_1$*/n*) and two polimorfic forms of a copper(II)complex (space groups *P-1* and *P2*$_1$*/n*) have been revealed and studied so far.

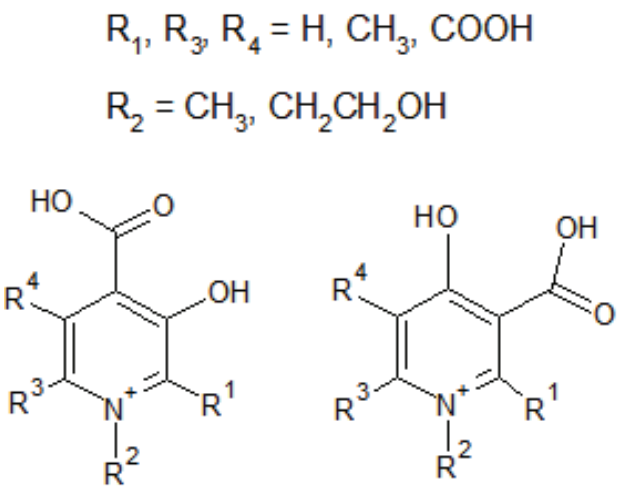

Figure 1. General formula of hydroxypyridinecarboxylic acid derivatives

Keywords: hydroxypyridinecarboxylic acid, chelat therapy, copper(II)complexes, secondary interactions