P23. Synthesis and Anti-proliferative Activity of Coordinative Combination of Copper, Cobalt, Nickel and Zinc with 2-acetylpyridine Semi- and Thiosemicarbazone and their 4-Phenyl Substituents

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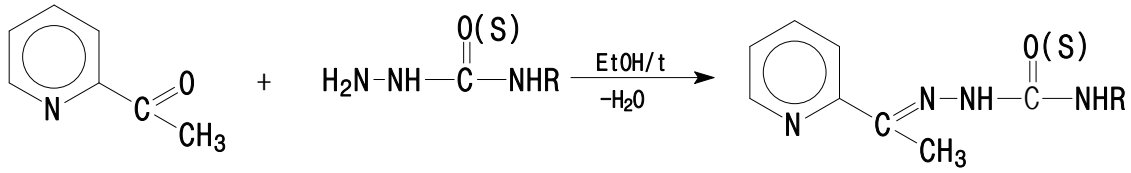
It is well known that many semi- and thiosemicarbazide derivatives display biologic activity and are widely used in medicine in treating infections caused by different microorganisms. Many of these substances form with the salts of transition metals coordination compounds that display physiological activity, and can be examined as preparations with biochemical and pharmacologic application. Thus, the synthesis and study of new coordination compounds of bio-metals with semi- and thiosemicarbazide derivatives are of scientific and practical interest.

The aim of the given paper is to establish optimum conditions of synthesis, structure, physicochemical and biological properties of cobalt, nickel, copper and zinc coordination compounds with semicarbazone (L^1), 4-phenylsemicarbazone (L^2), thiosemicarbazone (L^3), and 4-phenylthiosemicarbazone (L^4) 2-acetylpyridine.

First were synthesized the L^1-L^4 compounds, whose synthesis scheme can be presented in the following way:



where R=H, C_6H_5

Then, the interaction of ethanol solutions of chloride, bromide, copper (II) nitrate and sulphate with the L^1 – L^4, taken in 1:1 molar ratio led to microcrystalline substances for which the compositions $CuL^{1-4}X_2$ (X = Cl, Br, NO_3, $1/2SO_4$) were determined on the basis of elemental analyses data. However, when copper salts are replaced with chloride, bromide, nitrate, acetate of cobalt, nickel and zinc, the reaction results in substances with the composition $M(L^{1-4}\text{-}H)_2X$. Comparing the IR spectra of the initial semi- and thiosemicarbazones with those of the synthesized complexes showed that the L^{1-4} act as monodeprotonated tridentate N,N,O (for $L^{1,2}$) and N,N,S (for $L^{3,4}$) ligands and coordinate to central atoms through the atoms of pyridinic and azomethinic nitrogen and oxygen (for $L^{1,2}$) or sulphur (for $L^{3,4}$).

Furthermore, indentifying the anti-proliferative activity of the synthesized complexes was of high interest.

It was found that the copper complexes of these ligands inhibit the growth of myeloid leukemia cells, and that a 4-phenyl substituent increase the activity. For 4-phenyl semicarbazone 2-acetylpyridine high activity is also manifested for cobalt and nickel complexes (in comparison with the medicine - doxorubicine - used currently in the medical science for treating and preventing leucoses).

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