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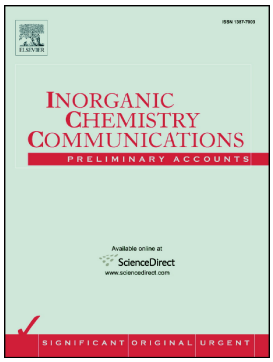

Synthesis, structural studies and antimicrobial activities of manganese, nickel and copper complexes of two new tridentate 2'formylpyridine thiosemicarbazone ligands

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Synthesis, Structural Studies and Antimicrobial Activities of Manganese, Nickel and Copper Complexes of Two New Tridentate 2-Formylpyridine Thiosemicarbazone Ligands

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Abstract

Two new thiosemicarbazone ligands {**HL^1** = 4-(2-chlorophenyl)-1-((pyridin-2-yl)methylene)thiosemicarbazide and **HL^2** = 4-(2-methoxyphenyl)-1-((pyridin-2-yl)methylene)thiosemicarbazide} were synthesized. With Mn^{2+}, Ni^{2+} and Cu^{2+}, the metal complexes $[Mn(L^1)_2]$ **1**, $[Ni(L^1)Cl]$ **2**, $[Cu(L^1)Cl]$ **3**, $[Mn(L^2)_2]$ **4**, $[Ni(L^2)Cl]$ **5** and $[Cu(L^2)Cl]$ **6** have been isolated and their structures were assigned based on their CHNS contents, magnetic moments, spectral (IR, UV-Vis) data and DMF solution molar conductivities. The complexes are of varied structures, spanning from octahedral manganese complexes to square planar nickel and copper complexes or even square pyramidal geometries and adopt different topologies, such as monomers or dimers. Further studies on complex **2** and **3** were performed; single crystals of **2** and **3** were grown and analyzed by XRD technique. Additionally the thermal degradation mechanism of **2** in nitrogen atmosphere has been studied, being observed the formation of nickel sulfide as a final product at temperature of around 700ºC. All ligands and complexes have been tested against fungal and bacterial cultures and, in many cases, the biological activity of the free ligands is enhanced upon coordination.

Keywords: Thiosemicarbazones, tridentate ligands, Schiff base complexes, Molecular structure, Antimicrobial activity.

1. Introduction

Since their introduction, thiosemicarbazones (TSCs) have attracted the attention of many researchers worldwide[1-3] due to their well-documented antitumoral[4,5], antiviral[6], antimicrobial[7], antitrypanosomal[8] and antimalarial[9] activities. In several instances, it has been reported that the TSCs' antimicrobial activity increases upon coordination with metal ions[10] offering the possibility of dose reduction[11-16]. Structurally, TSCs are a class of bidentate ligands that coordinate metal ions with formation of stable five-membered rings via their thiolate sulfur and hydrazinic nitrogen atoms and can act as both neutral and anionic ligands[17].

A sub-class of TSCs is that one derived from condensation of TSCs with 2-formylpyridine; in these ligands, the pyridine nitrogen atom is also able to coordinate metals inducing extra-stability to the final complexes by forming two fused five-membered rings. Interesting biological activities have been reported for 2-formylpyridine TSCs, being 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (Triapine) one of the most studied TSC compounds for cancer chemotherapy which included a number of clinical trials[18,19].

In the present article, we aim at exploring other 2-formylpyridine TSCs those would have interesting biological activities, therefore it is reported the synthesis of two new thiosemicarbazones, **HL^1** = 4-(2-chlorophenyl)-1-((pyridin-2-yl)methylene)thiosemicarbazide and **HL^2** = 4-(2-methoxyphenyl)-1-((pyridin-2-yl)methylene)thiosemicarbazide, as well as their respective metal complexes: {$[Mn(L^1)_2]$ **1**, $[Ni(L^1)Cl]$ **2**, $[Cu(L^1)Cl]$ **3**, $[Mn(L^2)_2]$ **4**, $[Ni(L^2)Cl]$ **5** and $[Cu(L^2)Cl]$ **6}**. The characterization of the metal complexes was performed using a variety of spectroscopic techniques, including XRD analysis in the case of complex **2** and **3** for which single crystals could be obtained. Finally, we report also the antimicrobial activity of all ligands against various fungal and bacterial cultures and how this activity is enhanced by complexation with the different metals.

2. Experimental

2.1. Materials and methods

The syntheses were conducted using as purchased high-purity chemicals and absolute solvents. 4-(2-chlorophenyl)thiosemicarbazide[20] and 4-(2-methoxyphenyl)thiosemicarbazide[21] were prepared following literature. The ligand melting points were determined in open capillaries and are reported uncorrected. CHNS contents were obtained on an elementar Analysensysteme GmbH - vario EL III Element Analyzer. Infrared spectra were recorded as KBr pellets in the region of 4000 - 400 cm^{-1} on a Nicolet iS10 spectrophotometer. Electronic spectral data of all ligands and complexes, in methylene chloride solutions, were measured on a Perkin Elmer UV/VIS spectrophotometer Lambda 40 using cuvettes of 1 cm matched silica in the range of 250 - 1000 nm. The NMR spectra were recorded on Bruker Avance III spectrometers operating at 400 and 300 MHz. ^1H and ^{13}C chemical shifts (δ) are