Palladium and platinum derived diacetylmonoxime thiosemicarbazone complexes of medicinal interest

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Introduction

Thiosemicarbazones (TSCs) and their transition metal complexes possess remarkable pharmacological properties including anti-neoplastic activity. On the other hand, oximes are well known due their use in the preparation of brain perfusion imaging agents like ⁹⁹ᵐTc-HMPAO (Ceretec). The combination of TSCs and oximes may lead to compounds with interesting biological properties.

PtII complexes, mainly cisplatin derivatives, are widely used in the treatment of a large number of cancer types. However, the efficacy of cisplatin is limited. In order to overcome these limitations, the development of platinum complexes that are structurally different to the classical cisplatin analogues is required. In addition, the chemical similarities of PdII (isoelectronic and isosteric) place this metal as first candidate to substitute PtII anticancer metallo drugs. In the present work we devote our interest to the coordination chemistry of an oxime TSC ligand system with PtII and PdII, aiming to obtain new anticancer agents.

Results and Discussion

The oxime thiosemicarbazone ligand (H₂otsc) was synthesized by refluxing diacetylmonoxime with one equivalent of ethylthiosemicarbazide. Reactions of [MC₂(H₂otsc)] (M = Pt or Pd) with H₂otsc under reflux in acetonitrile with base addition afford the analog complexes [M(PPh₃)(otsc)]H₂O (1 for M = Pd and 2 for M = Pt).

The complexes have been characterized by CHNS analysis, conductimetry, UV-Vis, FTIR, NMR (¹H and ³¹P) and by X-ray diffraction on single crystals.

The FTIR spectra of the complexes indicate the coordination of the ligand upon double deprotonation. The ¹H-NMR spectra of both complexes are very similar and present all the expected signals. The ³¹P{¹H} NMR spectrum of 1 consists of a sharp singlet signal at δ 27.64 ppm, while the spectrum of 2 shows a resonance at δ 17.02 ppm, with a J(¹⁸⁷P-³¹P) coupling of around 3700 Hz.

X-ray structure analyses confirm the spectroscopic data. Fig. 1 presents the molecular structure of the PtII complex, which is isostuctural with the PdII one, crystalizing in the trigonal crystal system, space group R3. The otsc²⁻ ligand binds the MII centers as N,N,S-chelate with double protonation. A considerable delocalization of r-electron density is evidenced in the five membered rings and is extended to the oxygen atom from the oxime moiety.

![Figure 1](image)

**Figure 1.** Crystal and Molecular Structure of [Pt(PPh₃)(otsc)]H₂O (2). The H atoms of the PPh₃ ligand and the H₂O molecule were omitted for clarity.

Conclusions

New PtII and PdII complexes containing an oxime thiosemicarbazone ligand have been prepared and fully characterized. The biologic potential of these complexes is of high interest and in vitro cytotoxic studies against tumor cells are now underway.

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