Área: INO

Orthopalladated oximes compounds containing 2,6-lutidine: Synthesis, structure, DNA binding studies and cytotoxic assays

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Highlights

New orthopalladated oximes active against tumor cells and low affinity toward DNA.

Resumo/Abstract

This work deals with the synthesis, structural characterization and antiproliferative effects of three novel Pd^{II} complexes (**1-3**) of the type [PdCl(C^2,*N*-L1)(luti)], [PdCl(C^2,*N*-L2)(luti)] and [PdCl(C^2,*N*-L3)(luti)], where L1 = acetophenone oxime, L2 = benzaldehyde oxime, L = tetralone oxime and luti = 2,6-lutidine, as potential antitumor agents. Compounds **1-3** have been fully characterized by elemental analysis and spectroscopic techiniques (FTIR and NMR). The crystal and molecular structures of **1-2** have been determined by X-ray diffraction analysis. In all the cases, it has been observed a nearly square planar environment around Pd atom composed by the *C,N*-donor atoms from cyclopalladated oxime, one N atom from lutidine and one chloro ligand. The N atoms are oriented in a *trans* configuration (Fig 1). All compounds have been screened against tumor cell lines (MCF-7, A549 and MDA-MB-231) and fibroblasts (MRC5) via MTT assays. In particular, complex **3** has exhibited cytotoxic effects against MDA-MB-231 (7.54 ± 0.33 μM) and MCF7 (IC_{50} = 14.78 ± 0.06 μM). Preliminar DNA binding studies on **3** have been carried out through spectrophotometric titrations and circular dichroism experiments. The increase of the concentration of **3** has not resulted in meaningful changes in the spectral CD profile of ct-DNA (Fig 2), indicating that the cyclopalladated establishes a weak interaction with DNA. Upon sucessive addition of aliquots of **3** to the DNA-Hoescht 33258 solution, a decrease of fluorescence intensity (*ca*. 10 %) has been detected (Fig 3), suggesting that **3** binds weakly to DNA.

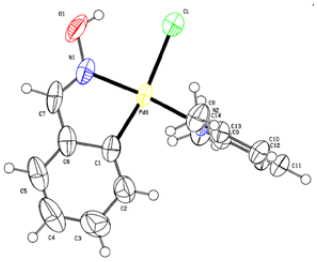

Fig 1. The molecular structure of **2**, showing the atom-labelling and displacement ellipsoids.

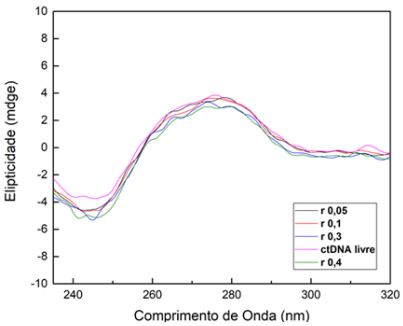

Fig 2. CD spectra of ct-DNA (85 μM) in Tris-HCl in the absence and presence of the palladium complex **3**.

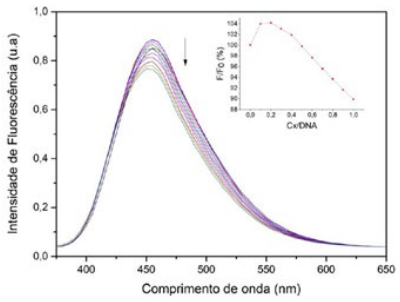

Fig 3. Fluorescence emission spectra for the Hoechst 33258 solution (λexcitation = 350 nm) with increasing amounts of the complex **3**.

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