

Half sandwich Ru(II) complexes containing acylthiourea ligands: structure, DNA/HSA-binding, and biological properties in breast tumor cell line

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Many non-platinum drugs have been evaluated against tumor cell, and ruthenium complexes are ones of the most successfully studied, two of them namely NAMI-A and KP1019/KP1339¹ entered to clinical trials, recently, organometallic “half sandwich” ruthenium complexes have showed promising anticancer agents and the complex RAPTA-C has shown moderate effects on solid tumor metastases². Taking into account, here we have synthesized and characterized eight metal complexes of this class, using acylthiourea ligands and their corresponding biological properties were explored. The complexes **1-8** (Figure 1, right) were obtained in good yields in which the reaction was carried out in methanol. The complexes have been characterized by satisfactory elemental analyses, IR, ¹H and ¹³C{¹H} NMR, UV-Vis spectroscopy, cyclic voltammetry, and X-ray for **1**, **2** and **3** (Figure 1b, left). All complexes exhibit growth inhibition on breast human tumor cells line MDA-MB-231, with IC₅₀ values between 6.0-37.0 μM. The most active compounds **5**, **6**, **7** and **8** were selected to continue the studies of morphology, clonogenic and wound healing assays. The results show that complexes are able to induces morphological changes, loss of adhesion, epithelial form and confluence, indicating the possibility of apoptosis³ and inhibit: i) the size and number of colonies and ii) the migration of the cells. The interaction of **5-8** with DNA measured by spectroscopic titration, viscosity, circular dichroism and gel electrophoresis, and HSA measured by spectrophotometric titration revealed that this biomolecules are an important target of action. Taken all together, the studies indicated that these metal complexes are potential agents against MDA-MB-231 tumor cells, encouraging us the continuation of studies of these types of compounds.

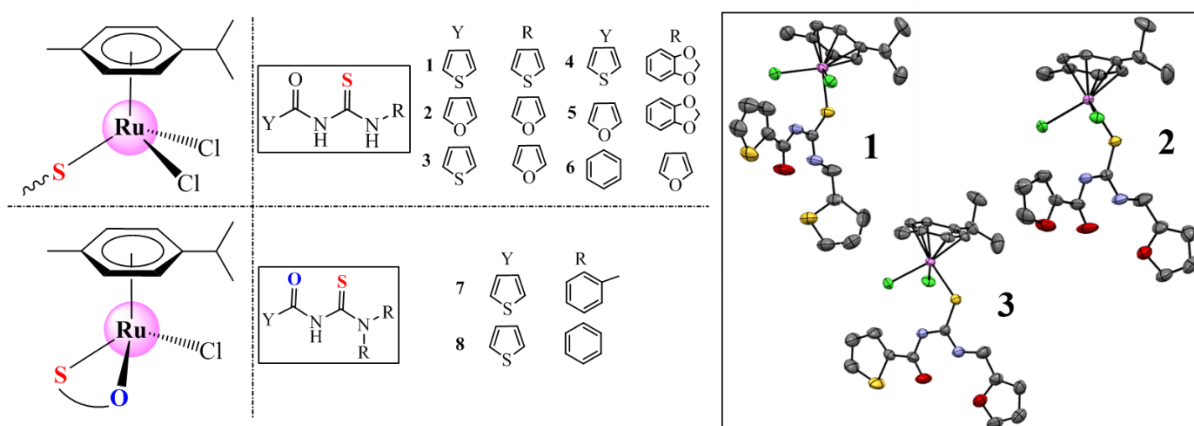


Figure 1. Right: General structure of half sandwich Ru(II) featuring acylthiourea. Left: ORTEP view of **1**, **2** and **3** showing the atomic labeling scheme and thermal ellipsoids at the 50% probability level.

¹Bergamo, A.; Sava, G.; *Dalton Trans.* **2011**, 40, 7817. ²Weiss, A.; Berndsen, R. H.; Dubois, M.; Muller, C.; Schibli, R.; Griffioen, A. W.; Dyson, P. J.; Nowak-Sliwinska, P.; *Chem. Sci.* **2014**, 5, 4742. ³Ziegler, U.; Groscurth, P.; *News Physio; Sci.* **2004**, 19, 124.

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