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The effect of Ru(II)-phosphine complexes on triple-negative breast cancer cells

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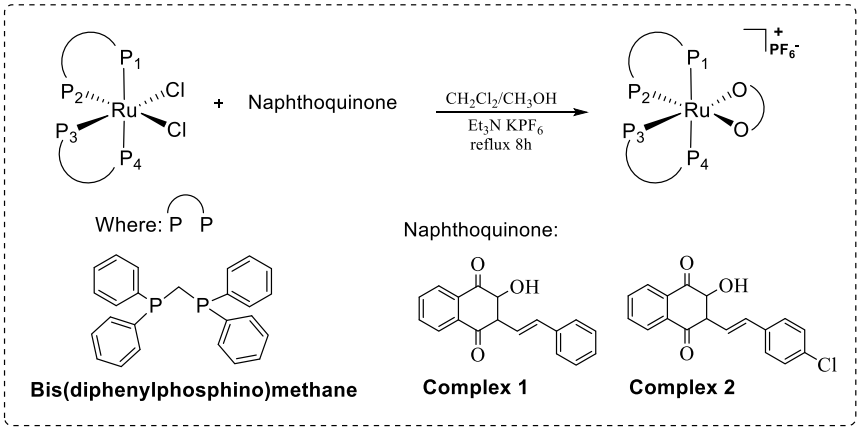
Highlights

- New ruthenium complexes containing naphthoquinone were synthesized and characterized.
- Ru^{II}-naphthoquinone complexes show potent anticancer activity against triple negative breast cancer cell lines.

Abstract

Breast cancer is a public health problem. Among the different types of breast cancer, triple-negative breast cancer is considered the most aggressive and has the worst prognosis. This makes the development of new metallodrugs extremely important. In recent years, ruthenium complexes have gained attention due to their potent antitumor activity. The aim of this work was to study new ruthenium(II) complexes containing naphthoquinone-derivative ligands for possible application as anticancer metallodrugs. Ru^{II}-naphthoquinone complexes identified as: (**1**) [Ru(**NQ1**)(dppm)$_2$]PF_6 and (**2**) [Ru(**NQ2**)(dppm)$_2$]PF_6 (where: dppm = *bis*(diphenylphosphine)methane)], **NQ1** = (E)-2-Hydroxy-3-styrylnaphthalene-1,4-dione; **NQ2** = (E)-2-(4-Chlorostyryl)-3-hydroxynaphthalene-1,4-dione), were synthetized from the precursor complex *cis*-[$RuCl_2$(dppm)$_2$] with the ligands derived from naphthoquinones, in dichloromethane/methanol (1:1), in the presence of triethylamine (**Scheme 1**). The complexes were characterized by elemental analyses, molar conductivity, UV–Vis, FT-IR, NMR and cyclic voltammetry. The crystal structure of complex (**1**) was determined by X-ray diffraction and their cytotoxicity against the MDA-MB-231 and MCF-7 breast cancer cell lines, and against the non-cancer cell line, the MCF-10A. Based on the $^{31}P\{^1H\}$ NMR spectra of compounds (**1**) and (**2**) in acetone-d6 it is classified into a typical ABMX spin system. The assay *in vitro* cytotoxicity of ruthenium complexes (**1**) and (**2**) was evaluated in human tumor and non-tumor cell lines using the MTS colorimetric assay. The compounds showed lower IC_{50} values than the reference drug cisplatin and the naphthoquinone ligands, suggesting high cytotoxic efficacy. The IC_{50} and selectivity index values were, respectively, IC_{50} = 0.11 ± 0.06 µM and SI = 9.6 for complex (**1**) and IC_{50} = 0.39 ± 0.04 µM and SI = 20.4 for complex (**2**).



Scheme 1. Synthetic route used to obtain ruthenium complexes (**1**) and (**2**).

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