Área: INO

Synthesis, characterization and cytotoxicity evaluation of new Manganese(II)/Naphthoquinone complexes

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Highlights

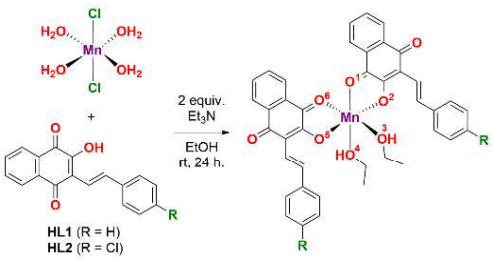
Two new Manganese(II)-Naphthoquinone complexes were obtained and their cytotoxicity investigated on different cancer cells.

Resumo/Abstract

2-Hydroxy-1,4-naphthoquinones are highly researched natural products, mostly due to their antitumoral, antibacterial, and antifungal activities.[1] These molecules are also recognized as good ligands for preparing bioactive metal-based complexes.[2] In this work, two new manganese(II) complexes containing stilbenes-quinone hybrids were synthesized and characterized. The key step in the synthesis of the naphthoquinone-stilbene hybrid ligands hydroxy-3-styryl-1,4-naphthoquinone **(HL1)** and 2-Hydroxy-3-(4-chlorostyryl)-1,4-naphthoquinone **(HL2)** was a ligand-free Heck reaction enabled by PEG-400, a green solvent that is able to stabilize the active Pd(0) catalyst, as a key step to building the naphthoquinone-stilbene hybrid structure. The complexes $[Mn(L1)_2(EtOH)_2]$ **(1)** and $[Mn(L2)_2(EtOH)_2]$ **(2)** were synthesized by the addition of ethanolic solutions of the corresponding deprotonated ligands to the Mn(II) precursor, with yields around 80%. FTIR spectra present, as example, ν(C=O) absorptions in 1647 cm^{-1} (HL1) and 1666 cm^{-1} (HL2) shifted to lower frequencies in **1** and **2**, indicating the *O*,*O*-bidentate coordination. An intense and broad band around 570 nm was observed in their UV-Vis spectra, attributed to intraligand $n \rightarrow \pi^*$ and MLCT transitions. DRX analysis revealed monoclinic and triclinic crystal system for **1** and **2**, respectively. The non-electrolytic nature of the complexes was supported by molar conductance measurements. Several molecular descriptors were calculated by molecular modeling approach. The charge distribution, dipole moments, and Gibbs free energy of the complexes were obtained, suggesting that the formation of **1** is approximately five times more favored than **2**. The cytotoxicity of both complexes and free naphthoquinone ligands were investigated against different cancer cell lines after 48 h of incubation via MTT assay. In general, the results presented in Table 1 indicates the coordination as a crucial strategy to increases the cytotoxicity potential of the naphthoquinone derivatives. The best results were obtained in A2780 ovarian cancer cells, leading selectivity indexes equal to 3.6 and 2.1, for 1 and 2, respectively (SI = IC_{50}MRC-5/IC_{50} A2780). Our results suggest **1** and **2** as promising metal-based compounds against ovarian cancer.

Table 1. *In vitro* cytotoxicity (IC_{50}, μM) results on A2780 (ovarian), A2780-*cis* (ovarian cisplatin resistant) and MCF-7 (breast) cancer cells, and MRC-5 (lung) non-cancerous cells after 48 h of incubation. Data are presented as mean ± SD of three independent replicates.

	A2780-cisR	***A2780***	***MCF-7***	***MRC-5***
1	14.05 ± 0.36	6.89 ± 0.87	30.79 ± 2.05	24.91 ± 1.16
2	8.95 ± 1.57	7.58 ± 0.37	30.29 ± 5.24	16.02 ± 2.33
HL1	36.90 ± 2.25	> 25	> 50	> 50
HL2	> 50	> 50	> 50	> 50
$MnCl_2$	> 50	> 50	> 50	> 50



Scheme 1. Complexation strategy to produce **1** and **2**.

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