Title: Synthesis, characterization, electrochemical behavior and in vitro protein tyrosine kinase inhibitory activity of the cymene-halogenobenzohydroxamato [Ru(eta(6)-cymene)(bha)Cl] complexes

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Abstract: The ruthenium(II)-cymene complexes [Ru(eta(6)-cymene)(bha)Cl] with substituted halogenobenzohydroxamato (bha) ligands (substituents = 4-F, 4-Cl, 4-Br, 2,4-F-2, 3,4-F-2, 2,5-F-2, 2,6-F-2) have been synthesized and characterized by elemental analysis, IR, H-1 NMR, C-13 NMR, cyclic voltammetry and controlled-potential electrolysis, and density functional theory (DFT) studies. The compositions of their frontier molecular orbitals (MOs) were established by DFT calculations, and the oxidation and reduction potentials are shown to follow the orders of the estimated vertical ionization potential and electron affinity, respectively. The electrochemical E-L Lever parameter is estimated for the first time for the various bha ligands, which can thus be ordered according to their electron-donor character. All complexes exhibit very strong protein tyrosine kinase (PTK) inhibitory activity, even much higher than that of genistein, the clinically used PTK inhibitory drug. The complex containing the 2,4-difluorobenzohydroxamato ligand is the most active one, and the dependences of the PTK activity of the complexes and of their redox potentials on the ring substituents are discussed. (C) 2012 Elsevier B.V. All rights reserved.

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