

Novel (μ -oxo)bis(μ -ibuprofenato)diruthenium(III) complexes derived from the reaction of the paddlewheel structured diruthenium-ibuprofen anticancer metallodrug with imidazole and 2-methyl-imidazole

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Our research group has investigated dimetallic carboxylates bearing the mixed-valence $\text{Ru}_2(\text{II,III})$ or Ru_2^{5+} core in the $[\text{Ru}_2(\text{O}_2\text{CR})_4]^+$ unit with paddlewheel arrangement in which four carboxylate ligands form equatorial bridges that stabilize Ru-Ru bonds with bond order 2.5. The coordination of the Ru_2^{5+} core to non-steroidal anti-inflammatory drugs (NSAIDs) mainly derived from phenylalkanoic acids such as ibuprofen has generated a novel class of metallodrugs with interesting pharmacological properties [1]. In order to elucidate crucial points for the activity of these compounds, the reactions of the Ru_2 -ibuprofen complex of formula $[\text{Ru}_2(\text{Ibp})_4\text{Cl}]$ with imidazole and 2-methyl imidazole were investigated. These *N*-heterocyclic bases are mimetic of the side chain of histidine, an important amino acid from the viewpoint of metal complexation in the biological level. They have σ -donor/ π -receptor dual character, and can bind firstly, mainly through σ -donation, to the axial positions of the tetracarboxylato-complex. The π -acid character seems to favor the migration of those ligands to the equatorial positions which show higher π -electron density, thus stabilizing the metal-ligand bond by π -backbonding. This backbonding decreases the electron density at the metal-metal bond to break the cage structure resulting in ruthenium complexes of the type $[\text{Ru}_2(\mu\text{-O})(\mu\text{-C}_{12}\text{H}_{17}\text{CO}_2)_2(\text{L})_6]^{2+}$, where L may be either the imidazole or 2-methyl imidazole, which contain one μ -oxo bridge, in similar way to other carboxylate complexes previously reported [2]. The products from the reaction of $[\text{Ru}_2(\text{Ibp})_4\text{Cl}]$ with both of the imidazole ligands were isolated as PF_6^- salts of bluish-purple color. The electronic spectra in ethanolic solution show bands at 563 and 561 nm which can be assigned to the $d\pi\text{-}p\pi$ transition characteristic of the μ -oxo complex of Ru(III). Charge transfer bands which probably involve the *N*-ligand and the metal were observed at 350 nm for both complexes. The molar conductivity value of $83 \Omega^{-1}\text{cm}^2 \text{mol}^{-1}$ suggests 2:1 electrolyte behavior in ethanolic solution. Vibrational bands at 1550 and 1394 cm^{-1} were assigned to the $\nu_a(\text{COO})$ and $\nu_s(\text{COO})$ stretching modes of the carboxylate group, respectively. The difference between the wavenumbers of the two stretching modes ($\Delta\nu$) was 156 cm^{-1} , corroborating the bridging coordinating mode of the carboxylate ligands [2,3]. The results from this study gave the first evidences that the formation of μ -oxo species from the diruthenium(II,III)-ibuprofen metallodrug might be favored in the presence of biomolecules containing imidazole groups in the physiological environment.

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