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Organorutenijumski(II)-halido kompleksi sa derivatima benzimidazola: sinteza i uporedna citotoksična studija

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Kompleksi rutenijuma predstavljaju najperspektivniju alternativu kompleksima platine koji se decenijama unazad koriste kao antikancerogeni lekovi. Stoga opisujemo sintezu i kompletnu karakterizaciju šest novih kompleksa $[(\eta^6\text{-}p\text{-cymene})\text{RuX}(\text{L}_{1,2})]$ gde je $\text{HL}_1 = 1H\text{-benzimidazol-2-karboksilna kiselina}$, $\text{HL}_2 = 5\text{-hloro-1}H\text{-benzimidazol-2-karboksilna kiselina}$, a $\text{X} = \text{Cl}^-$, Br^- , I^- . Citotoksičnost kompleksa je ispitana na ćelijskim linijama K562 i MRC-5.

Ru(II) kompleksi su dobijeni u reakciji dva ekvivalenta HL_1 , odnosno HL_2 sa ekvimolarnom količinom $[(\eta^6\text{-}p\text{-cymene})\text{RuX}_2]_2$ u etanolu na sobnoj temperaturi. Nakon četvorčasovnog mešanja, izolovan je finalni proizvod u vidu žuto-narandžastog taloga. Kompleksi su okarakterisani pomoću IC, NMR i MS spektrometrije, elementalne analize i rendgenske strukturne analize za $[(\eta^6\text{-}p\text{-cymene})\text{Ru}(\text{L}_1)]$ koji kristališe u $P2_1/n$ prostornoj grupi. Ru(II) jon je oktaedarski koordinovan za imidazolski atom azota i karboksilatni kiseonik potvrđujući konformaciju stolice tipičnu za ovaj tip kompleksa. Kompleksi sa I^- ligandom pokazuju umerenu, ali selektivnu citotoksičnost prema K562 ($IC_{50}([(\eta^6\text{-}p\text{-cimen})\text{Ru}(\text{L}_1)]) = 53.9 \pm 2.2 \mu\text{M}$ i $IC_{50}([(\eta^6\text{-}p\text{-cimen})\text{Ru}(\text{L}_2)]) = 83.97 \pm 3.85 \mu\text{M}$).

Organoruthenium(II)-halido complexes with benzimidazole derivatives: synthesis and comparative cytotoxic study

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Ruthenim complexes are the most promising alternative to platinum complexes which have been utilized as anticancer drugs decades ago. Thus we describe synthesis and full characterization of six new complexes $[(\eta^6\text{-}p\text{-cymene})\text{RuX}(\text{L}_{1,2})]$, where $\text{HL}_1 = 1H\text{-benzimidazole-2-carboxylic acid}$, $\text{HL}_2 = 5\text{-chloro-1}H\text{-benzimidazole-2-carboxylic acid}$, and $\text{X} = \text{Cl}^-$, Br^- , I^- . Cytotoxicity of the complexes was studied on K562 i MRC-5 cell lines.

Ru(II) complexes were obtained in a reaction of two equivalents of HL_1 or HL_2 with equimolar amount of $[(\eta^6\text{-}p\text{-cymene})\text{RuX}_2]_2$ in ethanol at r.t. After four-hour long stirring, the final product was isolated in a form of a yellow-orange precipitate. The complexes were characterized by IR, NMR and MS spectrometry, elemental analysis and X-ray diffraction analysis for $[(\eta^6\text{-}p\text{-cymene})\text{Ru}(\text{L}_1)]$, crystallizing in the $P2_1/n$ space group. The Ru(II) ion is octahedrally coordinated for imidazole nitrogen atom and carboxylate oxygen confirming "piano stool" conformation typical for this type of complexes. Complexes with I^- ligand show moderate but selective cytotoxicity towards K562 ($IC_{50}([(\eta^6\text{-}p\text{-cimen})\text{Ru}(\text{L}_1)]) = 53.9 \pm 2.2 \mu\text{M}$ and $IC_{50}([(\eta^6\text{-}p\text{-cimen})\text{Ru}(\text{L}_2)]) = 83.97 \pm 3.85 \mu\text{M}$).