Polyhedron

Volume 19, Issues 22â€“23, 15 November 2000, Pages 2319-2325

Toward a novel metal-based chemotherapy against tropical diseases.: Part 5. Synthesis and characterization of new Ru(II) and Ru(III) clotrimazole and ketoconazole complexes and evaluation of their activity against *Trypanosoma cruzi*

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https://doi.org/10.1016/S0277-5387(00)00495-2

Abstract

The complexes $RuCl_3(CTZ)_3Â·2CH_3OH$ (**1**) and $RuCl_3(KTZ)_2(H_2O)Â·2H_2O$ (**2**) were prepared by reaction of $RuCl_3Â·3H_2O$ with CTZ and KTZ, respectively, while $RuCl_2(KTZ)_2$ (**4**) was prepared by reaction of $RuCl_2(CH_3CN)_4$ with KTZ (CTZ=1-[(2-chlorophenyl)diphenylmethyl-1*H*-imidazole, and KTZ=*cis*-1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazine. All the complexes were characterized by NMR spectroscopy and for the paramagnetic species EPR spectroscopy was also employed.

The new compounds were tested for in vitro activity against cultures of epimastigotes of *Trypanosoma cruzi*, the causative agent of Chagas disease, and compared with $RuCl_2(CTZ)_2$ (**3**) (reported previously) in order to establish some structureâ€“activity correlations. At concentrations of $10^{â^'6}$ M (DMSO), all the complexes showed higher activity than the parental organic drug against the epimastigote form of the parasite, and Ru(II) complexes seem to be more active than their Ru(III) counterparts for a given nitrogen-donor ligand.

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Keywords

Ruthenium; Clotrimazole; Ketoconazole; Paramagnetic; Metal complexes; *Trypanosoma cruzi*; Chagas

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