XXI Brazilian Meeting on Inorganic Chemistry
X Brazilian Meeting on Rare Earths
III Workshop on Theoretical Bioinorganic Chemistry
Belo Horizonte, September 12 - 15th 2024

New Ru(II) polypyridinic complexes with the 6ain ligand as potential vasodilators

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Thematic Area: Biological Inorganic Chemistry

Keywords: Vasodilation, Ru(II) complexes, Nitric oxide

Nitric oxide (NO) is a major gasotransmitter involved in a wide range of physiological responses and plays an important role in the cardiovascular system [1]. In certain pathological conditions, endogenous NO production is impaired, necessitating exogenous NO supplementation. In this context, the present study aimed to synthesise two new Ru(II) complexes of the type *cis*-$[Ru(bpy)_2(6ain)X]^{n+}$, where bpy is the 2,2'-bipyridine ligand, 6ain is the 6-azaindole ligand and X is the NO^+ (nitrosyl) or NO_2^- (nitro) ligand, which are potential NO donors. The complexes were synthesised by a route analogous to that reported in the literature [2]. A single crystal X-ray diffraction pattern for the complex cis-$[Ru(bpy)_2(6ain)NO_2]PF_6$ (FOR076) was obtained (Figure 1A), confirming its formation. The acidic conversion of FOR076 to cis-$[Ru(bpy)_2(6ain)NO](PF_6)_3$ (FOR086) is supported by the presence of a peak at 1942 cm^{-1} in the FTIR spectrum. ^{1}H NMR, COSY and ^{13}C NMR spectroscopy, UV-Vis absorption spectroscopy and cyclic voltammetry further support the successful synthesis of the complex. Chemical reactivity experiments indicate that only FOR086 is susceptible to chemical or electrochemical reduction with release of NO. Vasodilation assays in rat aorta (Figure 1B) indicate that both complexes act as potent vasodilators, with vasodilator potencies (pD2) estimated at 6.51 and 6.34 for $RuNO_2$ and RuNO, respectively. The cytotoxicity studies in H9c2 cells indicate that FOR076 and FOR086 are not toxic even at high concentrations (EC50>100 µM). This may overcome the limitations of SNP, which is effective but has high toxicity associated with CN release.

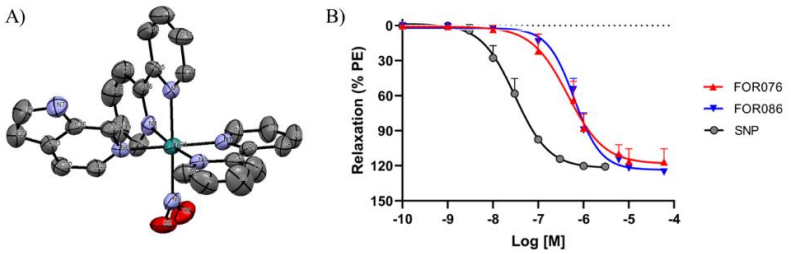

Figure 1. A) Single-crystal diffraction pattern of FOR076 and B) relaxation curves for the complexes FOR076, FOR086, and SNP.

Acknowledgments: CNPQ, CAPES, FUNCAP, FIOCRUZ-BA and CENAUREMN

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