

New precursor to nitrosyl trinuclear ruthenium complexes: developing new synthetic routes

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Introduction. Since Endothelium Derived Relaxing Factor (EDRF) was discovered, the interest in studying nitric oxide (NO) increases everyday motivated by its properties such as neurotransmission, vasodilation, anticancer activity and antiparasitic action¹. In view of that, nitrosyl trinuclear ruthenium complexes seems to be a reasonable choice as NO donors, since NO can be released under chemical/electrochemical reduction or light stimulus. In the particular case of nitrosyl trinuclear ruthenium complexes, there are at least three electrochemical processes achievable in biological medium, and the photorelease of NO can happen in the visible region². Given the importance of this class of complexes, efforts cannot be saved to optimize the synthetic route to obtain the precursor $[\text{Ru}_3\text{O}(\text{CH}_3\text{COO})_6(\text{CH}_3\text{OH})_3](\text{CH}_3\text{COO})$ (1) with an acceptable purity, since the classical route leads to a crude material contaminated with large amounts of NaCH_3COO and its purification leads to very low yields. Compound (1) is a key precursor to synthesize $[\text{Ru}_3\text{O}(\text{CH}_3\text{COO})_6(\text{CH}_3\text{OH})_2\text{NO}](\text{CH}_3\text{COO})$ (2), the new nitrosyl complex presented in this work. Up to now, precursor (2) has never been described. Through the original method², five steps are needed before the nitrosyl complex (2) is obtained, among them generation of $\text{CO}_{(\text{g})}$ (using $\text{H}_2\text{SO}_{4(\text{conc})}$ and H_3COOH) and $\text{Br}_{2(\text{g})}$ oxidation. The new synthetic route proposed in this work employs only three steps under milder conditions. **Experimental Section.** Compound (1) was synthesized using 0.50 g (1.16 mmol) of $\text{K}_3[\text{RuCl}_6]$ as ruthenium source (instead of using $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$, the classical precursor³), which was dissolved in 5 mL of hot water. In a 50 mL round-bottom flask, 0.50 g (5.09 mmol) of KCH_3COO was dissolved in a mixture of 15 mL of methanol and 10 mL of acetic acid and the solution was heated until 68 °C, when the aqueous solution of $\text{K}_3[\text{RuCl}_6]$ was added. The medium goes from reddish-brown to greenish-blue in 35 minutes at that temperature. After this period, the reaction medium was dried using a rotative evaporator. Complex (2) was obtained by dissolving that crude extract in 5 mL methanol, and then, the solution was diluted with 15 mL of dichloromethane. NO was bubbled 6 h in the resulting solution, which was kept in ice bath. The gas was generated *in situ* by adding HNO_3 30% to Cu^0 pellets, in a closed system maintained under argon atmosphere during all the experiment. After the 6 hour period, complex (2) is ready to proceed with ligand change in the two solvated positions. **Results and discussion.** Absorption spectra recorded to complex (1) obtained under the new synthetic conditions, showed a cleaner spectral profile with resolved bands and better baseline - the IC band splits into two components (619.5 and 677 nm) and the CT band appears at 391.5 nm. This ensures that the complex presents an acceptable purity to continue on nitrosyl synthesis without previous purification. In the case of (2), the spectral profile matches those presented by other nitrosyl trinuclear ruthenium complex: 441.5 nm (CT), 530 nm (CT), 670 nm (IC). Besides that, infrared spectrum confirmed the presence of coordinated NO because it's strong stretching band in 1880 cm^{-1} . **Final remarks.** The new nitrosyl complex was successfully obtained by a faster route, without the need of using dangerous reactants such as $\text{H}_2\text{SO}_{4(\text{conc})}$ and $\text{Br}_{2(\text{g})}$, and by using the pure precursor (1), obtained by the introduction of modifications in the classical route, as described in this work.

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