Synthesis and Reactivity of Ruthenium S-Nitrosothiol Complexes

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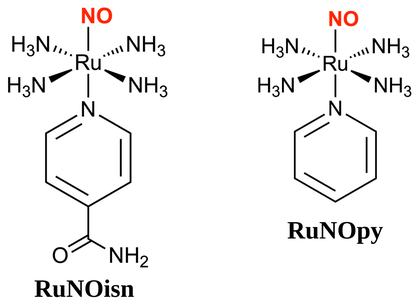
Introduction

The study of reactive species can be very complicated due to their short lifetime. In some cases, this issue can be mediated by improving the species' stability through coordination to a metal center. In this way, ruthenium tetra-amine complexes have been used for decades to help better understand the reactivity of Nitric Oxide (NO). [1] This can be accomplished by adjusting the electronic environment of the bound NO, by changing the ligand in *trans* position to it. In this way, we can further study the influence of the electronic environment on the reaction of interest, under different experimental conditions. The NO ligand can be attacked by a nucleophile, generating a stable adduct that can be studied under different experimental conditions. Previous work showed the coordination of an unstable species – $N(O)SO_3$ – to a ruthenium(II) center, obtained from the nucleophilic addition reaction of SO_3^{2-} with a ruthenium nitrosyl complex.[2] The purpose of this project is to investigate the reactivity between ruthenium-NO complexes and the nucleophiles cysteine and glutathione. Different *trans* ligands were used in order to study its influence on reactivity and stability. My results also shed further light on the mechanism of how the nitrosyl complexes react with the nucleophile:

$$trans\text{-}[RuNO(L)]^{3+} + SR^- \rightarrow trans\text{-}[RuNO(SR)(L)]^{2+}$$
$$trans\text{-}[RuNO(SR)(L)]^{2+} + SR^- \rightarrow trans\text{-}[RuNO(SR)_2(L)]^{+}$$

Ruthenium Nitrosyl Complexes



RuNOisn

RuNOpy

Fig 1. Structures of the Ru-nitrosyl complexes with the *trans* ligands isonicotinamide (**RuNOisn**; left) and pyridine (**RuNOpy**; right).

Nucleophiles

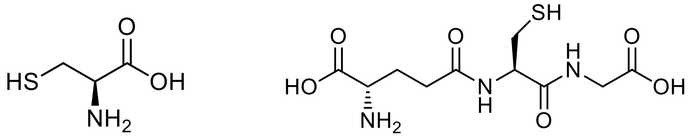


Fig 2. Structures of the nucleophiles Cysteine (left) and Glutathione (right).

Reactivity

UV-vis Spectroscopy

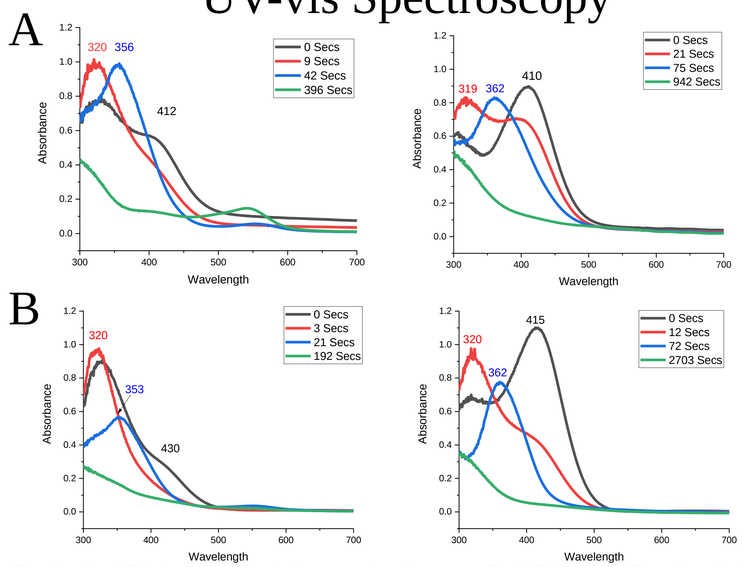


Fig 3. **A**. UV-vis spectra of the reaction between **RuNOisn** and Cysteine (left) and Glutathione (right). **B**. UV-vis spectra of the reaction between **RuNOpy** and Cysteine (left) and Glutathione (right). C_{Ru} = 0.5 x10^{-3} M; C_{Nu} = 50 x 10^{-3} M. Phosphate Buffer, 100 x10^{-3} M, pH 7.4.

Nuclear Magnetic Resonance (NMR)

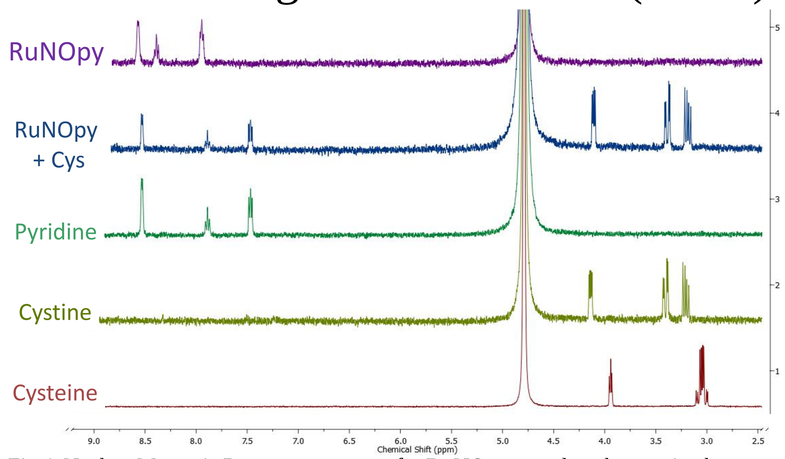


Fig 4. Nuclear Magnetic Ressonance spectra for **RuNOpy** complex, the reaction between **RuNOpy** and Cysteine, Pyridine Cystine, Cysteine. C_{Ru} = 1 x 10^{-3} M; C_{Cys} = 2.5 x 10^{-3} M. C_{py} = 1 x 10^{-3} M. Phosphate Buffer, 100 x 10^{-3} M, pH 7.4.

Infrared Spectroscopy

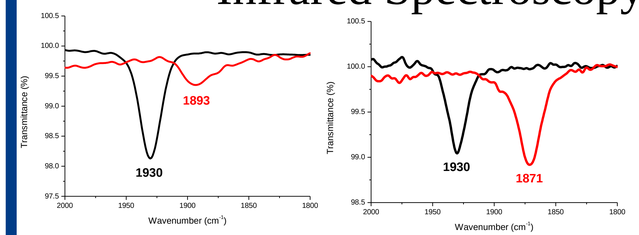


Fig 4. Infrared spectrum of **RuNOisn** (left) and **RuNOpy** (right) before (black) and after reaction with Cysteine (red). C_{Ru} = 50 x 10^{-3} M, C_{Cys} = 0.5 x 10^{-3} M. Phosphate Buffer, 1 M, pH 7.4.

Proposed Mechanism

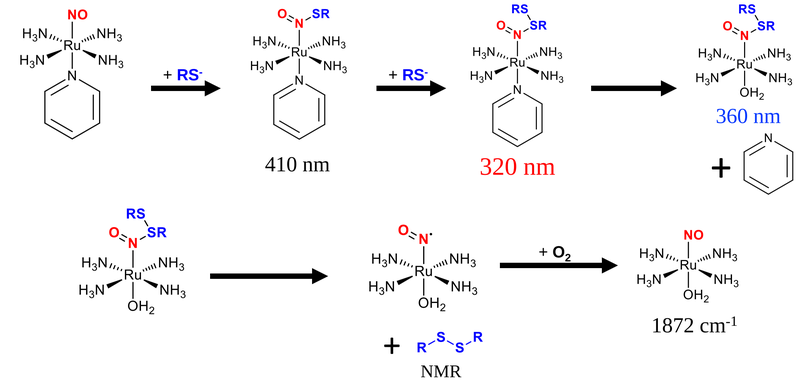


Fig 5. Proposed mechanism for the two consecutive nucleophilic additions to the **RuNOpy** complex

Density Functional Theory (DFT)

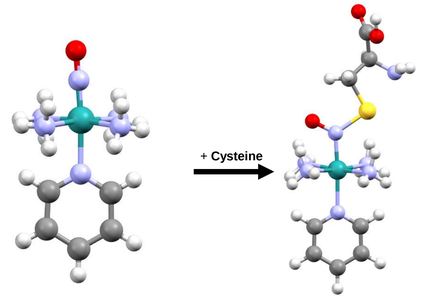


Fig 6. Optimized structure of the complexes using the functional BP86. RuNOpy (right) optimized using def2-TZVP basis set. The product of the first nucleophilic addition of Cysteine (right) was optimized using 3-21g basis set.

Conclusions

- Ruthenium nitrosyl complexes react with nucleophiles, allowing two consecutive additions.
- The product lead to labilization of the *trans* ligand, as observed by NMR.
- The disulfide product is also labilized from the complex, leading to the final aqua-nitrosyl ruthenium complex.

References & Acknowledgements

1. Souza, M. L., Roveda Jr. A. C., Pereira, J. C. M., Franco, D. W. New Perspectives on the Reactions of Metal Nitrosyls with Thiolates as Nucleophiles. *Coord. Chem. Rev.* **306**, 615-627, 2016.
2. Roveda Jr. A. C. *et al*. Light-activated Generation of Nitric Oxide (NO) and Sulfite Anion Radicals ($SO_3^{\bullet-}$) from a Ruthenium(II) Nitrosylsuphito Complex. *Dalton Trans.* **48**, 10812-10823. 2019.

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