Towards stable organometallic scaffolds for ^{211}At radiolabelling

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Motivation

- **Astatine-211 (^{211}At) holds potential for use in targeted alpha therapy of diseases like cancer.**
- **To maximize specificity of radioactive payload, tumor-specific compounds – typically organic compounds – are radiolabeled with ^{211}At.**
- **^{211}At seems ill-suited to make strong bonds with many organic scaffolds [1] causing release of radioactive payload to healthy body tissue.**
- **At is predicted behave similarly to iodine, which forms strong bonds with organometallic centers like rhodium and gold.**
- **Our aim is to explore Rh(I) and Au(I) centers for ^{211}At radiolabeling.**

Synthesis

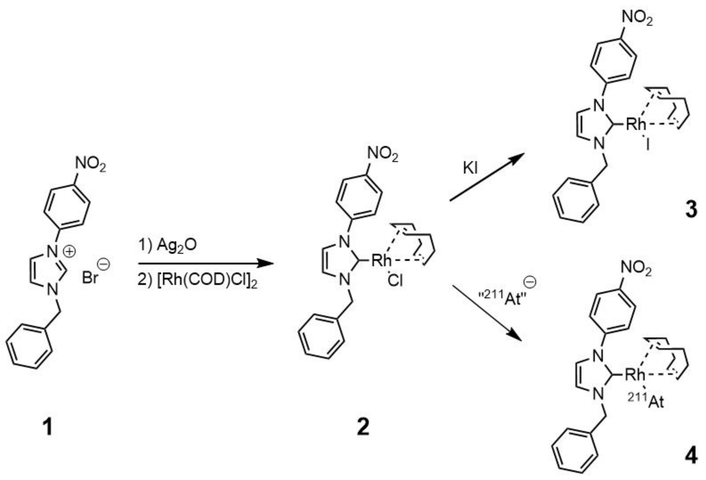

Figure 1. Synthesis of Rh(I) precursors **1-3** and radiolabelled **4**.

- **Compounds 1-3 [2] successfully synthesized and characterized by NMR spectroscopy and mass spectrometry.**
- **Chloride-iodide exchange models radiolabelling**
- **Synthesis of corresponding Au(I) compounds unsuccessful via this route.**

Crystal Structures

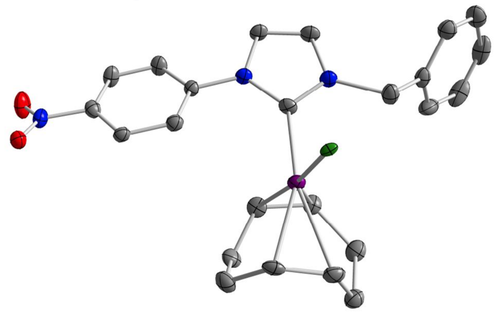

Figure 2. Crystal structure of **2**. Hydrogens are omitted for clarity.

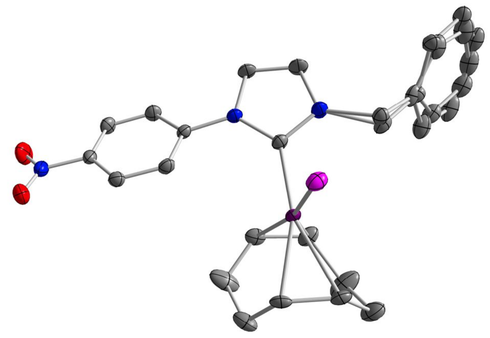

Figure 3. Crystal structure of **3**. Hydrogens are omitted for clarity.

- **Molecular structure of 2 and 3 determined by X-ray crystallography.**

Geometry Optimization Calculations

- **Model Rh-At and Au-At complexes were calculated by density functional theory**
- **Computed Rh-At distance: 2.81 Å; Au-At distance: 2.67 Å**
- **Calculations currently ignore spin-orbit coupling and relativistic effects**

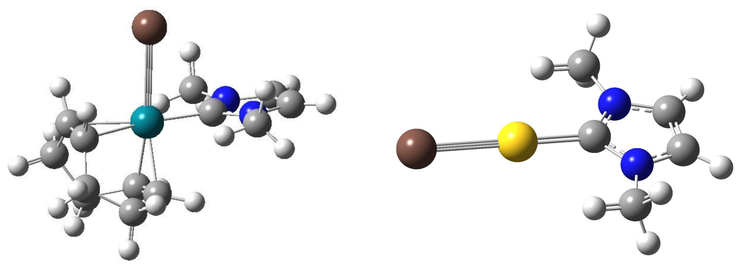

Figure 4. Computed structures of Rh-At (left) and Au-At (right) complexes.

Radiochemistry

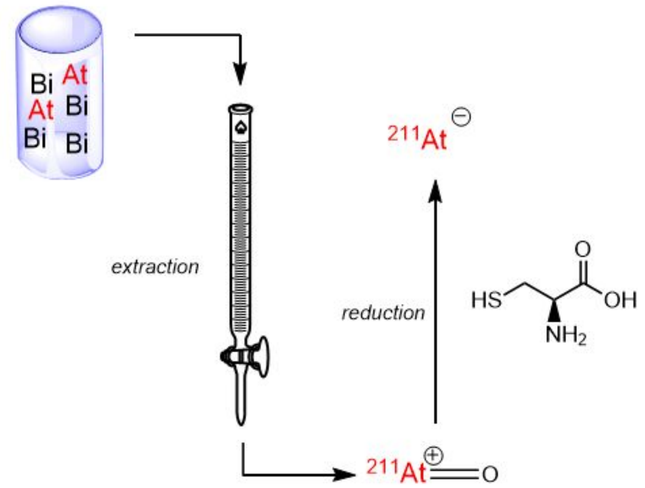

Figure 5. Production of ^{211}At for reactions with soft metal centers.

- **^{211}At=O extracted from ^{209}Bi target [3].**
- **Reduced to ^{211}At^{-} by cysteine and reacted with metal center [2].**
- **Radiochemical yield is determined by radioHPLC.**

Conclusions

- **Organometallic scaffolds seem promising as candidates for ^{211}At radiolabelling.**
- **Future work includes more rigorous calculations, isolation of Au(I) compounds, and modeling radiolabeling kinetics by UV-Vis spectroscopy.**

References

[1] D. Teze, *et al*. "Targeted radionuclide therapy with astatine-211: Oxidative dehalogenation of astatobenzoate conjugates." Scientific Reports

[2] H. Rajerison, *et al*. "Radioiodinated and astatinated NHC rhodium complexes: Synthesis." Nuclear Medicine and Biology

[3] J. D. Burns, *et al*. "Rapid recovery of At-211 by extraction chromatography." Separation and Purification Technology (2021).