Development of Novel Ferrocene-Based Gold Complexes for Anticancer Applications

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Introduction

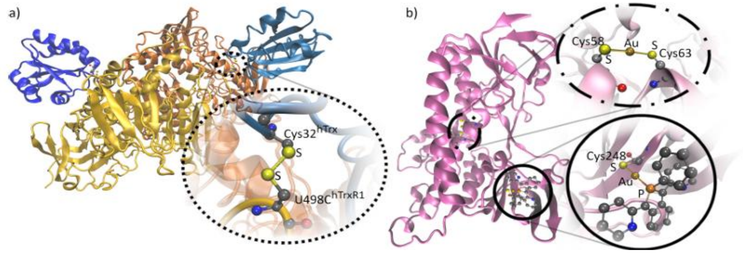
The United Nations Sustainable Development Goals provide a global framework for addressing major societal challenges and promoting a healthier and more sustainable future for all. Among these goals, SDG 3: Good Health and Well-being focus on reducing mortality from non-communicable diseases, including cancer, through the development of safe and effective therapeutic strategies.

Cancer remains a major global health challenge, and despite notable advances in chemotherapy, treatment options continue to be limited by severe side effects and inadequate selectivity, necessitating the development of novel therapeutic agents.

Metal-based N-heterocyclic Carbene (NHC) compounds have emerged as promising alternatives due to their unique mechanisms of action and tunable physicochemical properties

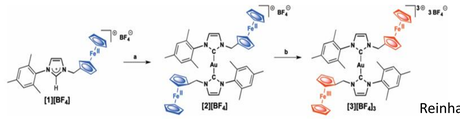
In particular, ferrocene derivatives exhibit exceptional redox stability and biological activity, while gold complexes have demonstrated significant potential as anticancer agents through mechanisms such as enzyme inhibition and disruption of cellular redox balance

Figure 1. Structure and Inhibition of Thioredoxin Reductase (TrxR)
(a) Normal structure of TrxR showing the essential selenocysteine–cysteine (Se–S) catalytic bond
(b) Binding of a gold complex to cysteine residues, forming Au–S bonds that inhibit enzyme activity



This study aims to design and synthesize a series of novel ferrocene-based NHC mono gold complexes as potential anticancer agents

Previous Synthetic Work



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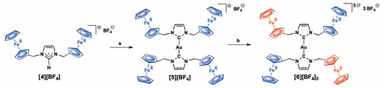

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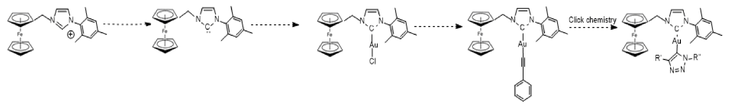
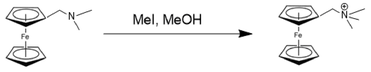
This work

Scheme 1. Synthetic route to proposed Au(I) complexes

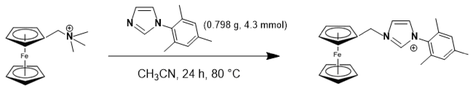


Current Results

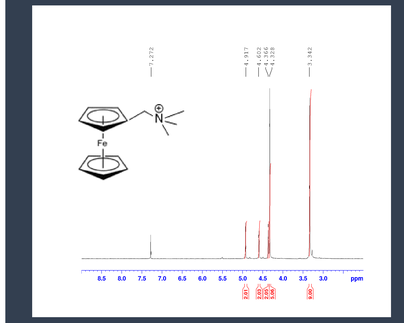
Scheme 2. Synthesis of Ferrocenylmethyl)-3-mesityl-imidazolium iodide

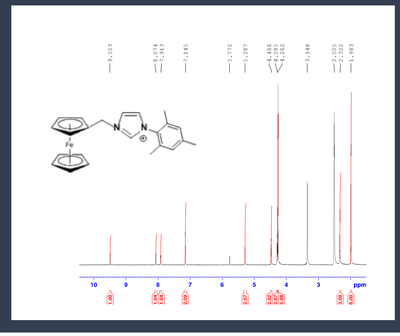


Scheme 3. Synthesis of 1-(Ferrocenylmethyl)-3-mesityl-imidazolium iodide



Characterization

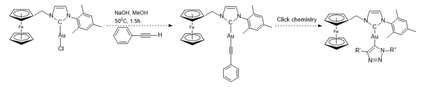




Future Directions

Scheme 4. Complexation to form the ferrocene–NHC–Au(I) complex

Scheme 5 Proposed substrate scope of ferrocene–NHC–gold complexes for



Conclusion

Synthesis of 1-(ferrocenylmethyl)-3-mesityl-imidazolium iodide has been completed. This compound will serve as the precursor for the preparation of the corresponding NHC ligand. The next steps of this work will involve generation of the NHC ligand and subsequent coordination to Au(I) to produce the corresponding ferrocene-NHC gold complexes. This synthetic strategy is expected to provide an efficient route to obtain the target compounds in good yield and purity. The resulting ferrocene-NHC-gold complexes are anticipated to be readily modified to generate a variety of functional derivatives, offering significant potential for applications in medicinal chemistry, particularly in the development of novel anticancer agents.

References

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2.Reinhard, G. L.; Jayaraman, S.; Prybil, J. W.; Arambula, J. F.; Arumugam, K. *Dalton Trans.*, **2022**, *51*, 10997–11006.

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