Macrocyclic Chromophores as a Novel Class of Fluorescent Molecules

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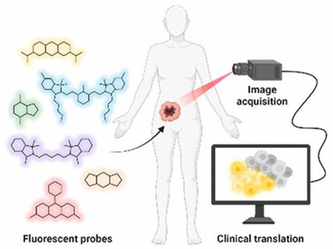
Introduction

Fluorescence imaging is a versatile technique for observing biological targets and visualizing biological processes in real time

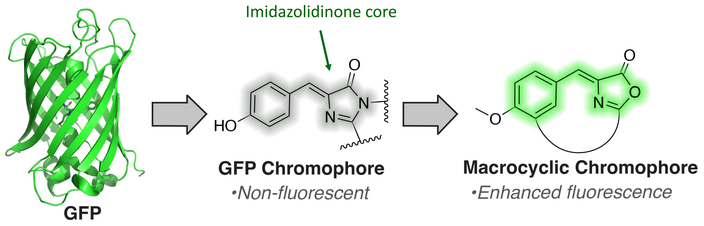
Green Fluorescent Protein (GFP) possess intrinsic fluorescence



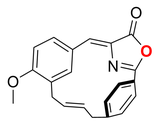
Vendrell, M et al., *ACS Nano,* **2023**, *17* (20), 19478–19490.

Hoffman, R., *Laboratory Investigation,* **2015**, *95*, 432–452.

Rotational freedom of the GFP chromophore reduces fluorescence emission→ limited ability for development as a general scaffold for fluorescence-based imaging techniques

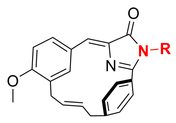


Macrocyclization can be used to restrict the free rotation of the chromophore to enable fluorescence outside of the protein environment



Synthetically feasible core

Synthetically feasible oxygen compound may have different optical properties than the natural imidazolidinone-based chromophore



GFP-based core

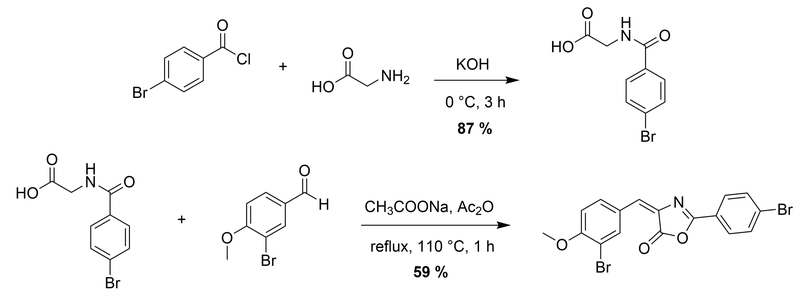
Nitrogen-swapping installs a tunable nitrogen functional group → easily optimizable for versatile small molecule GFP-based probes!

Aims

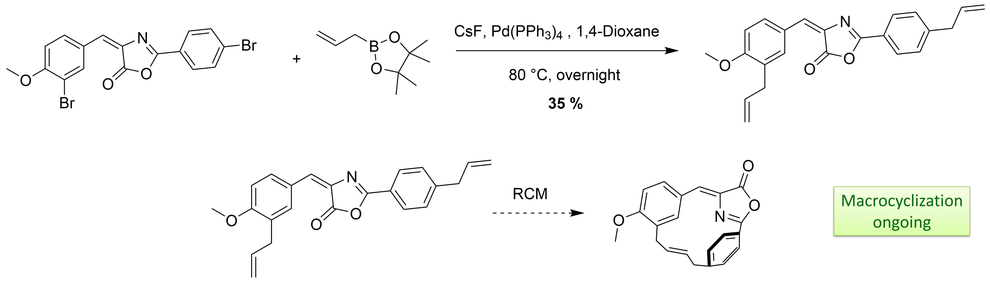
- Synthesize macrocyclic imidazolidinone derivative
- Perform nitrogen-swapping reaction to synthesize and characterize nitrogen-containing derivative
- Characterize structural and optical properties of synthesized molecules using NMR, UV-Vis, and fluorescence spectroscopy
- Characterize optical properties of synthesized molecules in glycerol solutions with varying viscosities

Results and Discussion

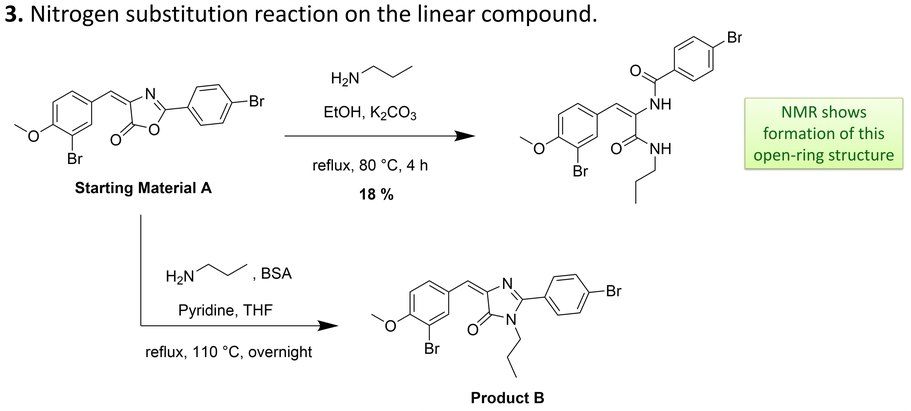
Stage 1. Synthesis of starting materials to prepare the GFP core.

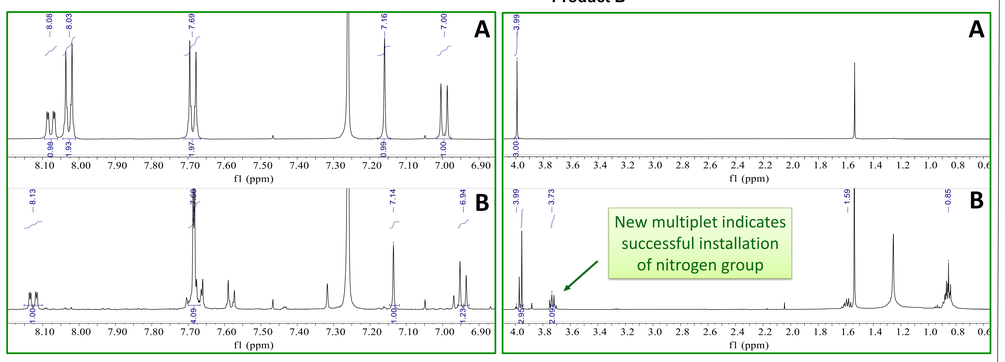


Stage 2. Synthesis of a GFP Chromophore-based macrocycle.

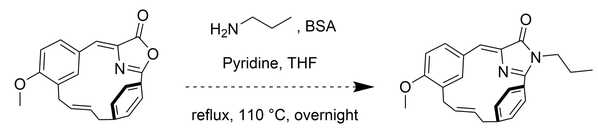


Stage 3. Nitrogen substitution reaction on the linear compound.



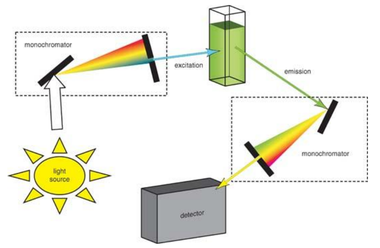


Stage 4. Nitrogen substitution reaction on macrocyclic structure.



Future Directions

- UV-Vis and fluorescence spectroscopy to characterize optical properties
- Characterization of fluorescence in glycerol solutions
- Evaluate optical properties of fluorophores in live cells
- Incorporate various backbones for macrocycle optimization



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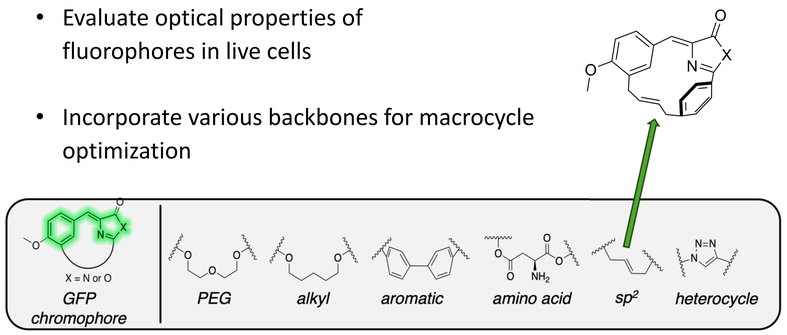

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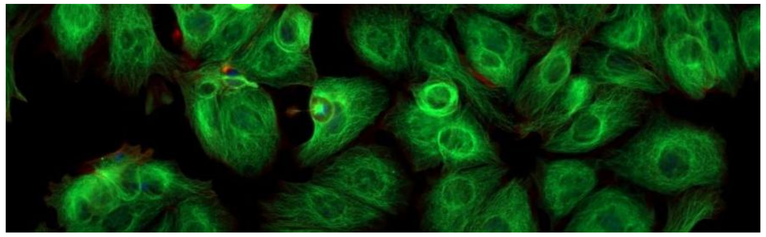
Conclusions

This research has the potential to advance design of novel fluorophores for high-resolution cellular imaging and improve our understanding of biological processes in living systems!



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