



# Macrocyclic Chromophores as a Novel Class of Fluorescent Molecules



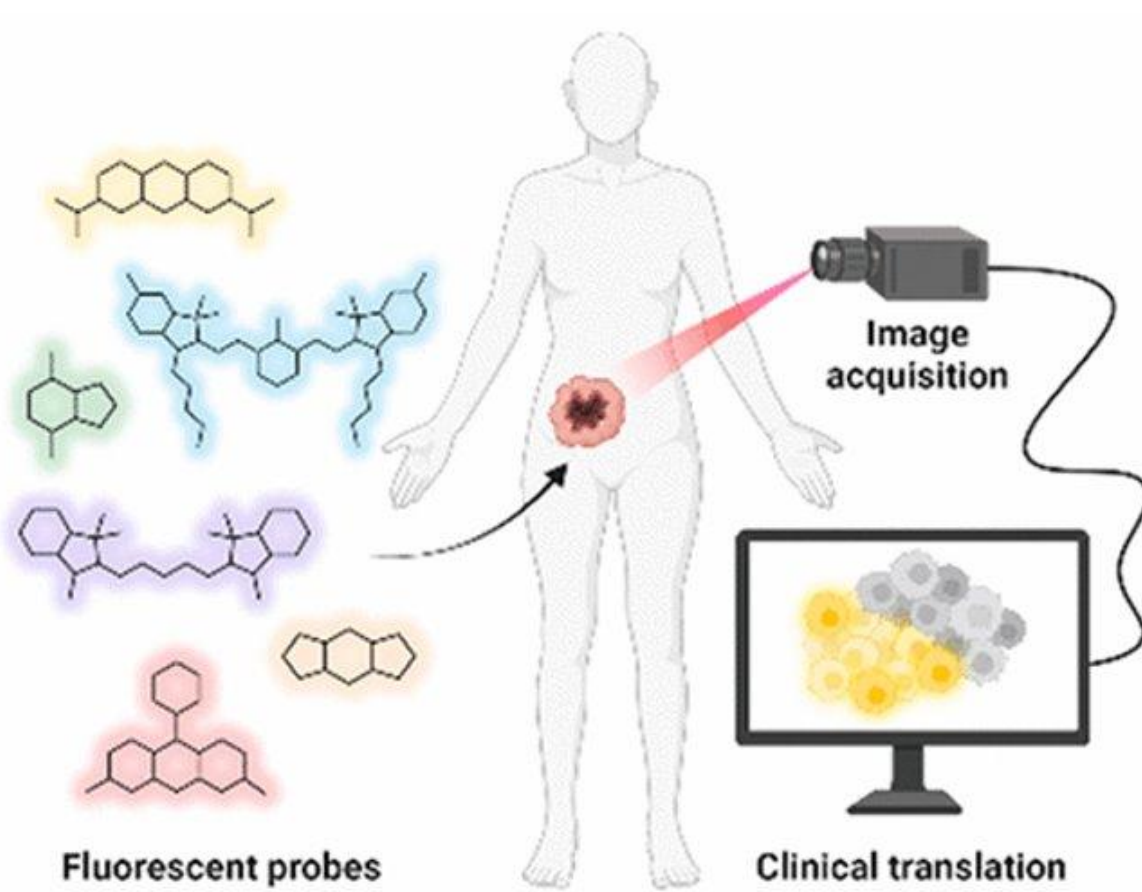
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## Introduction

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

**Green Fluorescent Protein (GFP)** possess intrinsic fluorescence

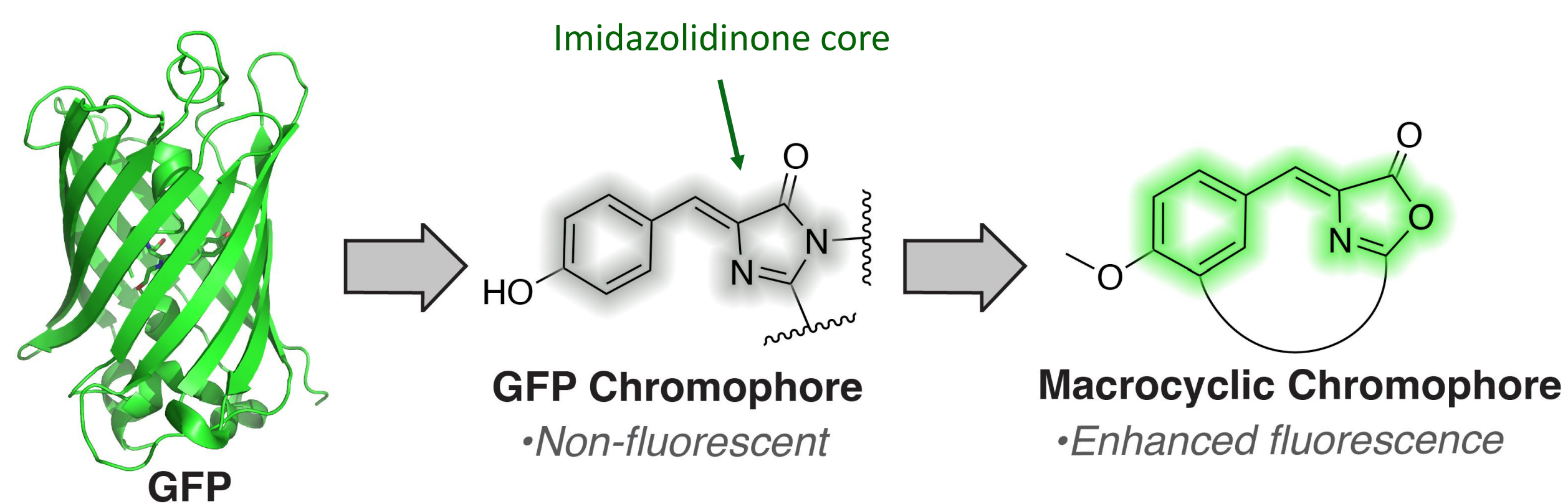


Vendrell, M et al., *ACS Nano*, **2023**, *17* (20), 19478–19490.

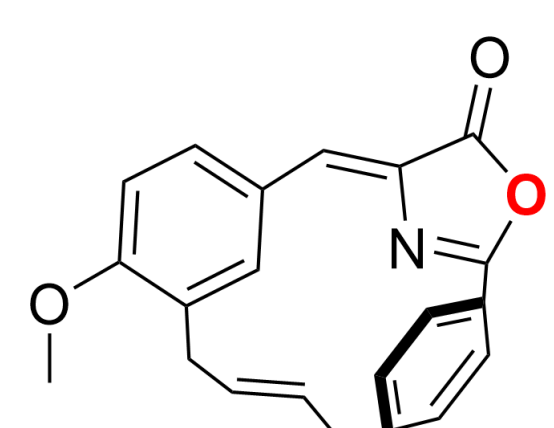


Hoffman, R., *Laboratory Investigation*, **2015**, *95*, 432–452.

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

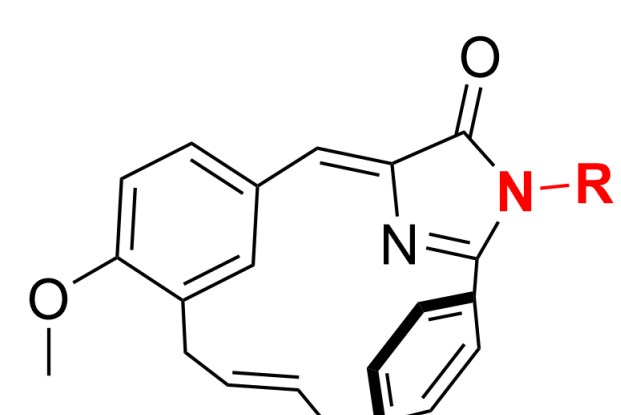


**Macrocyclization** can be used to restrict the free rotation of the chromophore to enable fluorescence outside of the protein environment



**Synthetically feasible core**

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



**GFP-based core**

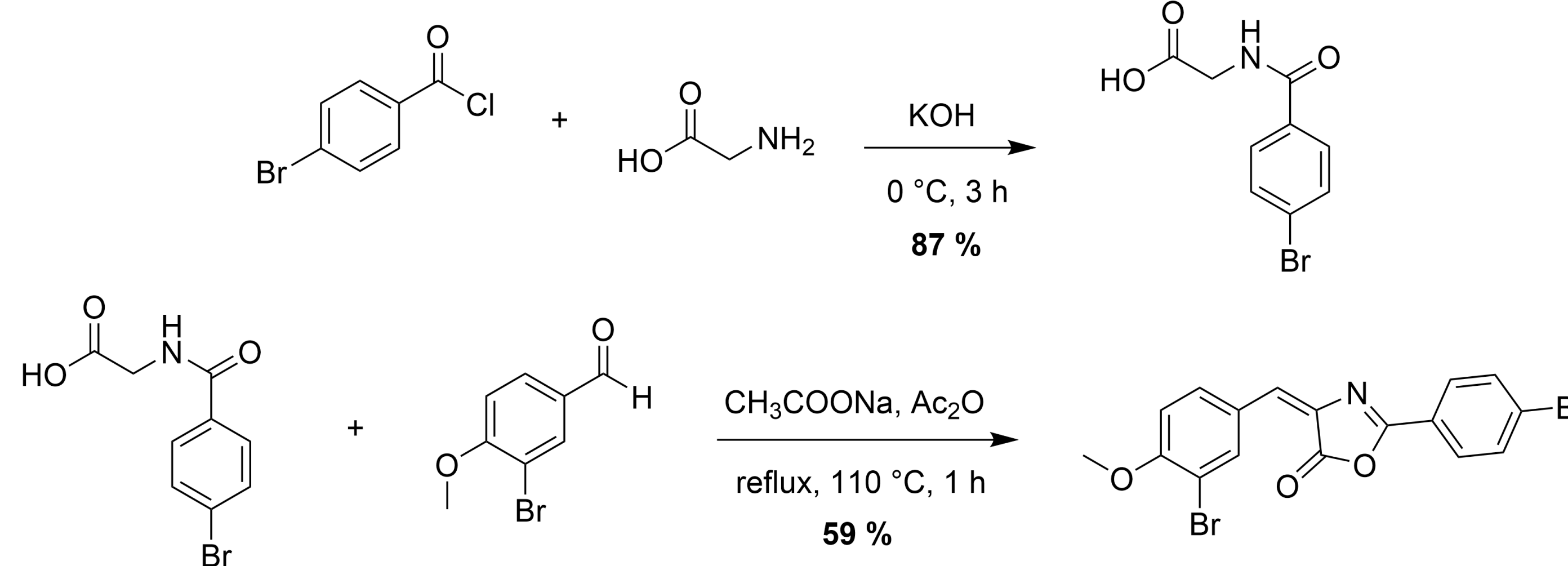
**Nitrogen-swapping** installs a tunable nitrogen functional group → easily optimizable for versatile small molecule GFP-based probes!

## Aims

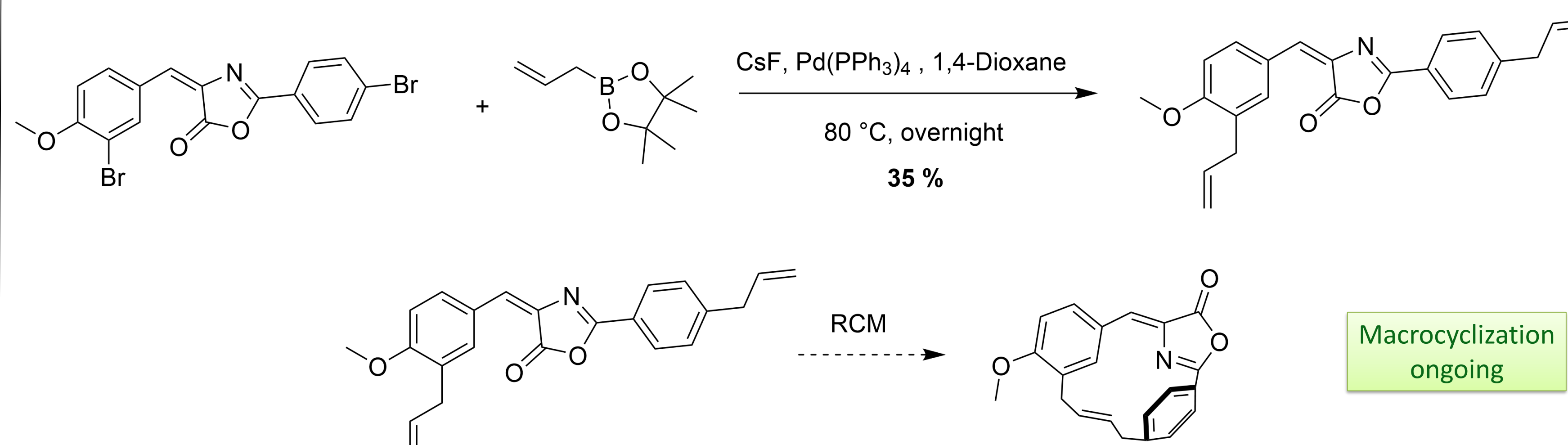
- Synthesize macrocyclic imidazolidinone derivative
- Perform nitrogen-swapping reaction to synthesize and characterize nitrogen-containing derivative
- Characterize structural and optical properties of synthesized molecules using NMR, UV-Vis, and fluorescence spectroscopy
- Characterize optical properties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

## Results and Discussion

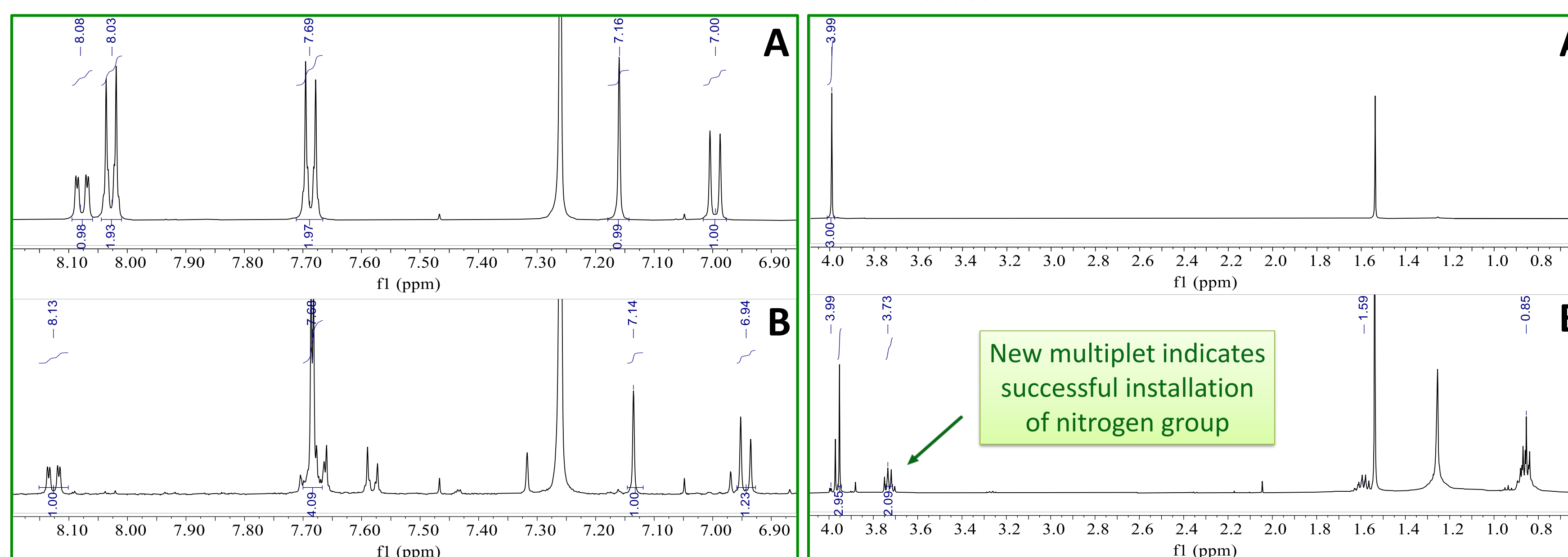
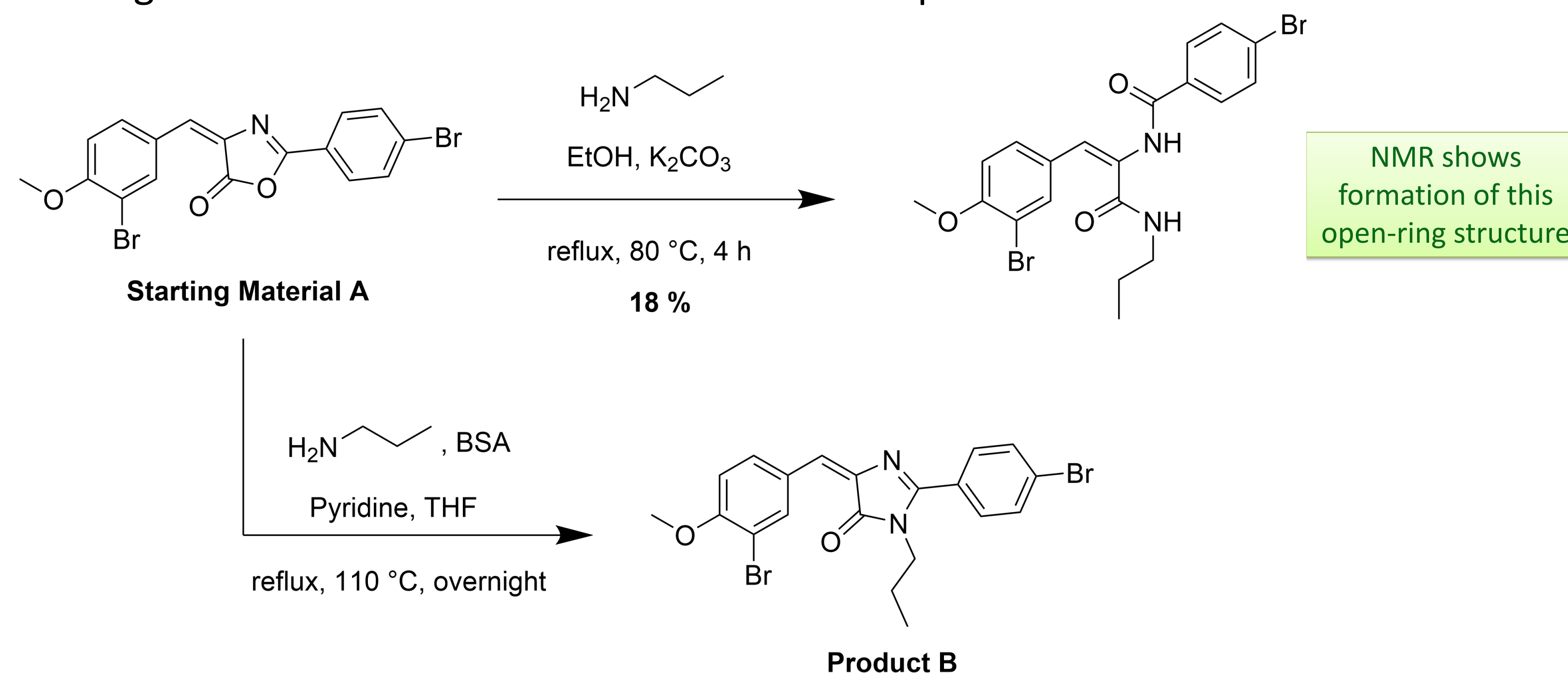
**Stage 1.** Synthesis of starting materials to prepare the GFP core.



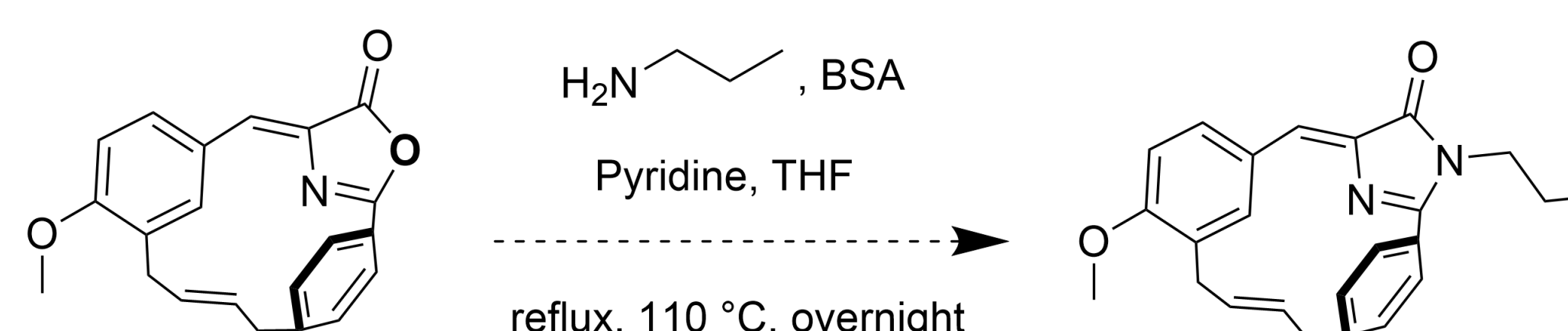
**Stage 2.** Synthesis of a GFP Chromophore-based macrocycle.



**Stage 3.** Nitrogen substitution reaction on the linear compound.

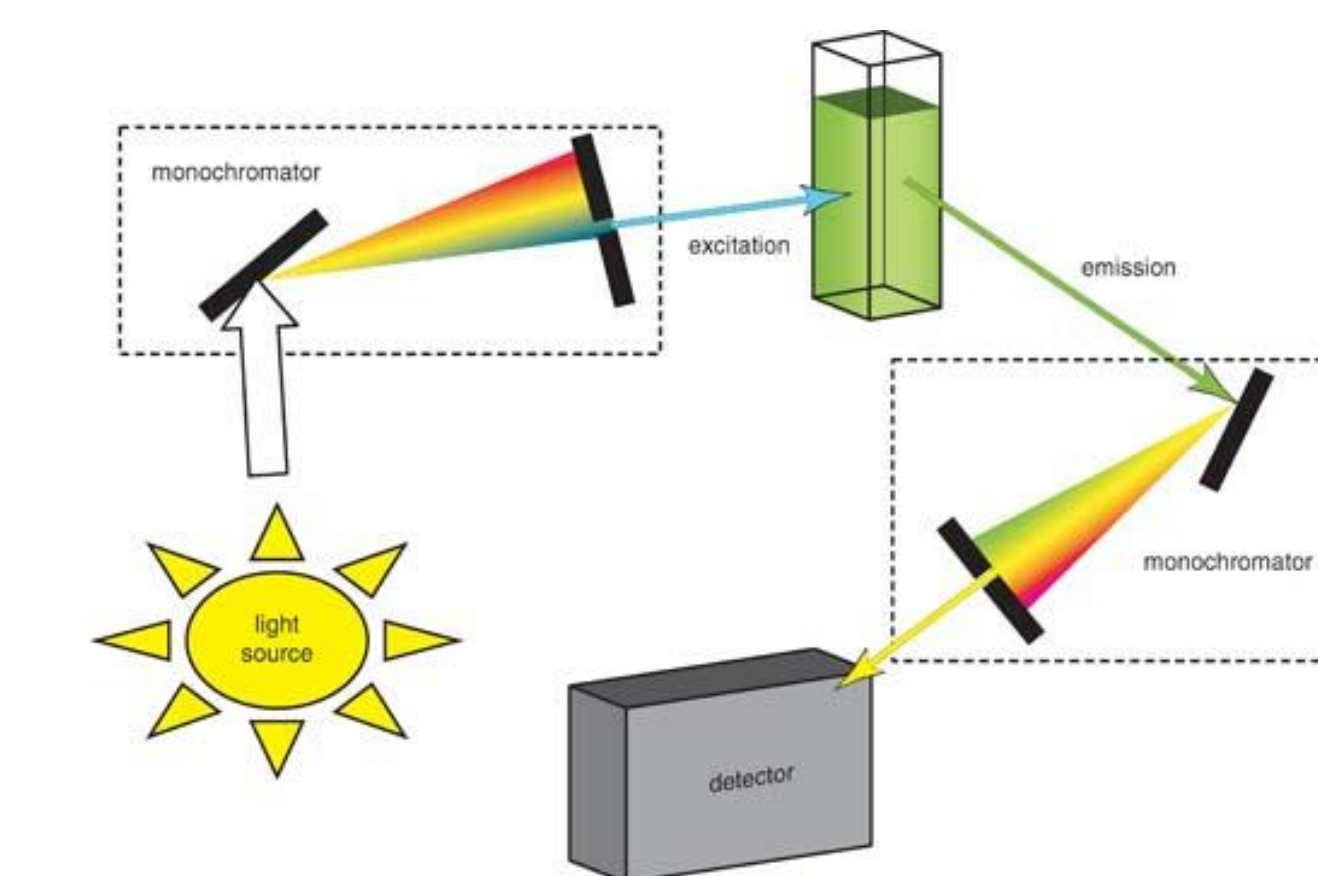


**Stage 4.** Nitrogen substitution reaction on macrocyclic structure.

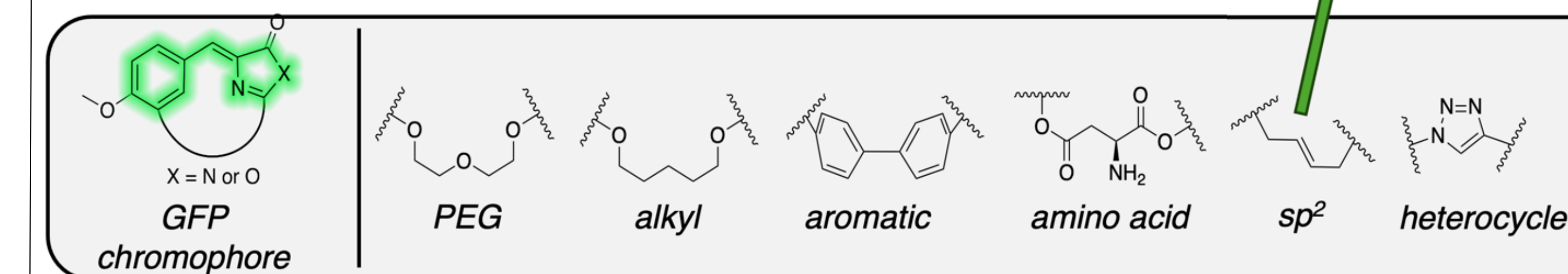
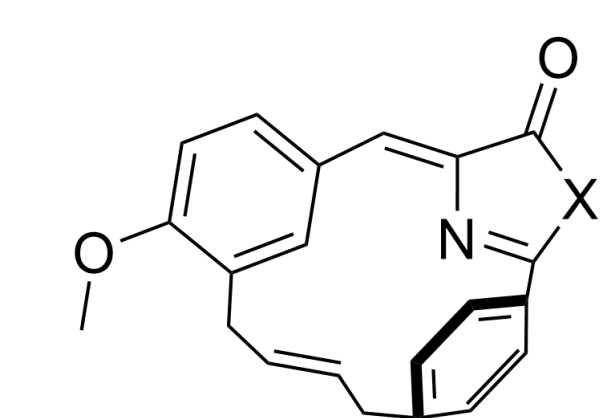


## Future Directions

- 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



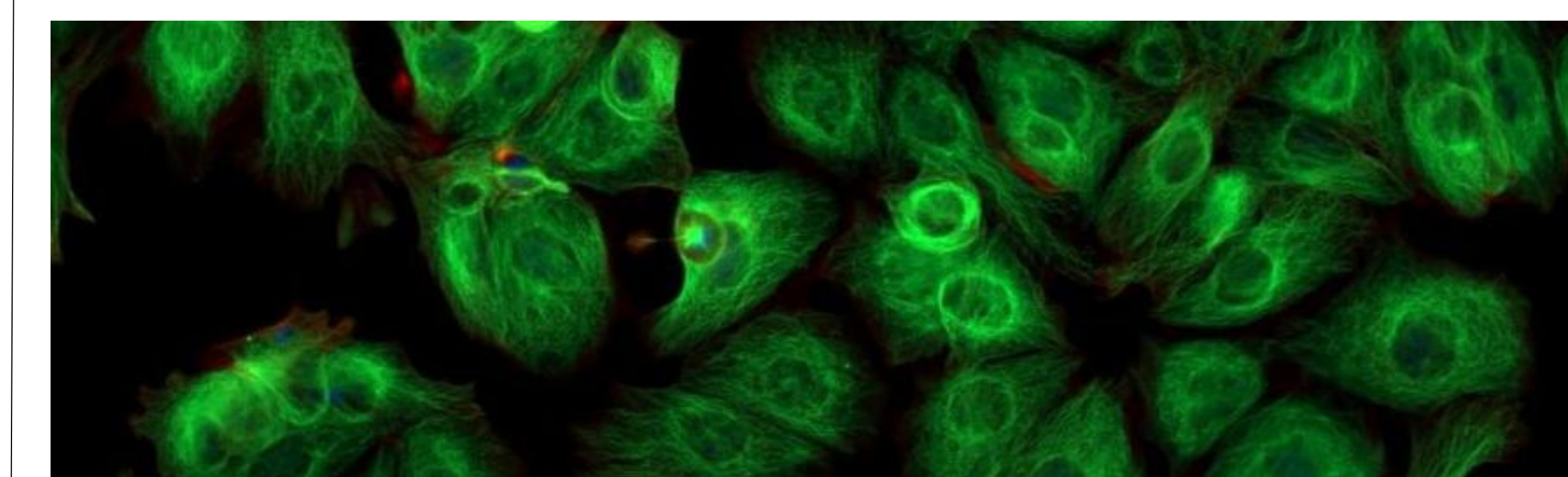
Raja, P. et al., *Fluorescence Spectroscopy*.



Choudhary, A. et al., *Protein Sci*, **2012**, *21* (2), 171-177.

## 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!



Fluorescent Proteins: Advantages and Disadvantages. *FluoroFinder*, **2022**.

## Acknowledgements

**Principal Investigator:**  
Dr. Brittany White-Mathieu

**Postdoc:**  
Dr. Aakriti Garg

**Graduate Students:**  
Arpan Ghosh  
Thomas DiPhilippo  
Saghar Jarollahi  
Paige Ring  
Prasanna Ganesh  
Yağmur Altunsoy

**Undergraduates:**  
Aliyah Krestalica  
Madison Pageau  
Mason Russel  
Nicholas Mixon  
Samuel Moreau



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