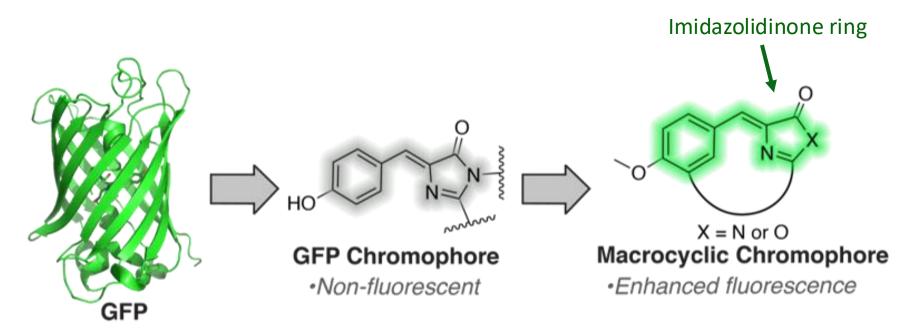


Macrocyclic Chromophores as a Novel Class of Fluorescent Molecules Muriel Lubelczyk*, Brittany White-Mathieu, Saghar Jarollahi Chemistry Department, University of New Hampshire, Durham, NH 03824

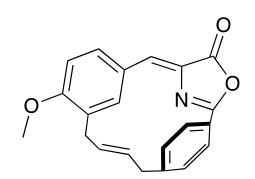
Introduction

Green Fluorescent Protein (GFP) is extremely useful in biological imaging techniques that enable the observation of cells and biological processes.

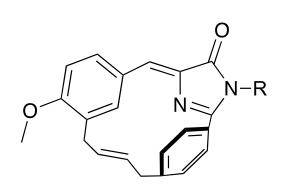


The ability to develop this chromophore of GFP as a general scaffold for advanced fluorescence-based imaging techniques is limited due to the rotational freedom of the molecule that induces fluorescence emission

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



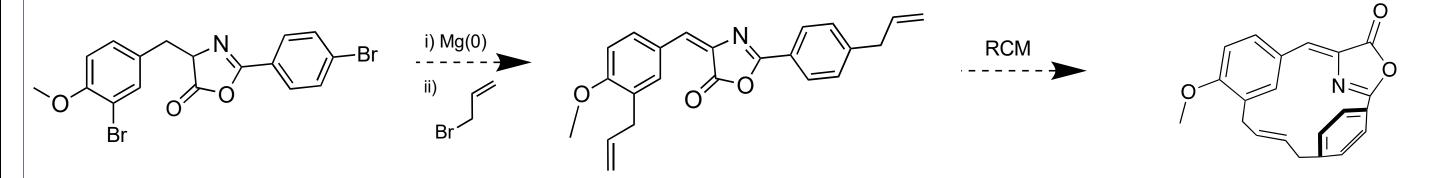
Synthetically feasible **GFP** core



GFP-based core

Optical properties of proposed imidazolidinone derivatives may not accurately represent the optical properties of the fluorescent protein chromophore due to differences in the structures of each compound

Characterization of the optical properties using UV-Vis and fluorescence spectroscopy will allow comparison of the oxygen and nitrogen containing macrocycles to the known properties of GFP.

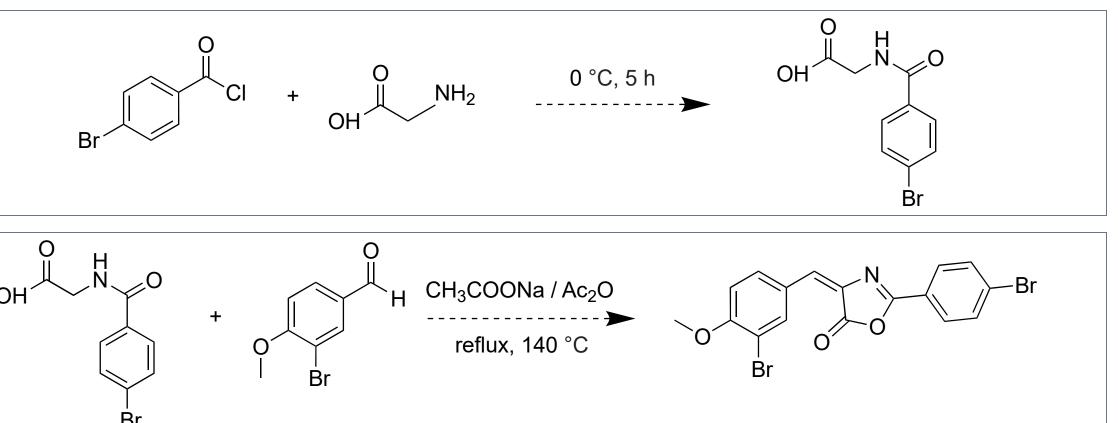


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Methods

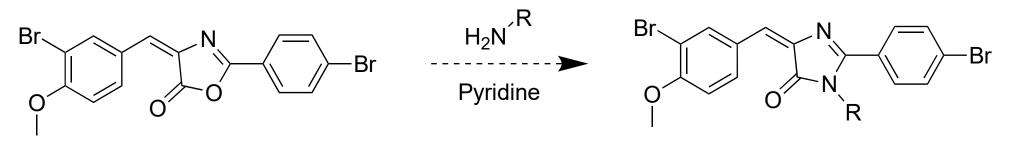
The following reactions have not been personally performed but were previously developed and validated by the White-Mathieu Lab.

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

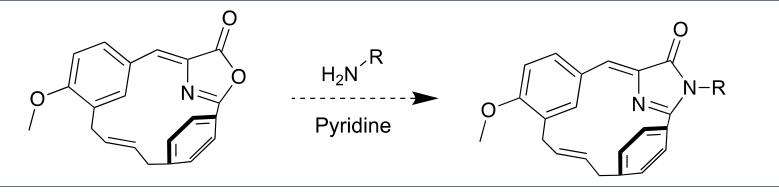


Stage 2. Synthesis of a GFP Chromophore-based macrocycle.

Stage 3. Nitrogen substitution reaction of the linear compound.



Stage 4. Nitrogen substitution reaction on macrocyclic structure.



Stage 5. Characterization of synthesized molecules.

NMR Spectroscopy

- Confirm structure and purity of each compound

UV-Vis Spectroscopy

- Determine absorption maximum wavelength

- Calculate molar absorptivity

Fluorescence Spectroscopy

- Determine emission maximum wavelength

- Calculate quantum yield

Characterization using glycerol

- Examine synthesized molecules in glycerol solutions with different viscosities

- Assess how viscosity affects fluorescence, both in linear and macrocyclic structures

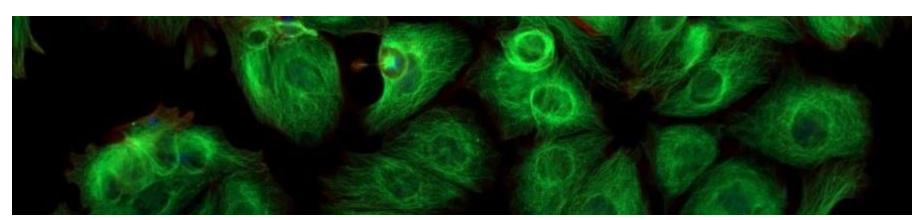


Aims

- Synthesize macrocyclic imidazolidinone derivatives
- 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
- Perform nitrogen swapping reaction to synthesize and characterize nitrogen-containing derivative

Conclusions

This research has the potential to present monumental contributions to our current biological imaging strategies, allowing us to expand applications of GFP chromophore analogs in biological imaging and develop macrocyclic fluorophores as tools to enhance fluorescent ability.



https://fluorofinder.com/newsletter-fluorescent-proteins-advantages-and-disadvantages/

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Undergraduates: Erin McCarthy Nicholas Mixon Taylor Stock Kylie Armor Madison Pageau

References

- (1) Veber, D. F.; Johnson, S. R.; Cheng, H.-Y.; Smith, B. R.; Ward, K. W.; Kopple, K. D. Molecular Properties That Influence the Oral Bioavailability of Drug Candidates. J. Med. Chem. 2002, 45 (12), 2615–2623. https://doi.org/10.1021/jm020017n.
- (2) FluoroFinder. Newsletter: Fluorescent Proteins: Advantages and Disadvantages. FluoroFinder. June 20, 2022. https://fluorofinder.com/newsletter-fluorescent-proteins-advantagesand-disadvantages/