Development of a Nanohoop Rotaxane For Sensing Reactive Oxygen Species

Phyllis Liao

Department of Chemistry and Biochemistry, Research Mentors: Ramesh Jasti and Claire Otteson

Introduction

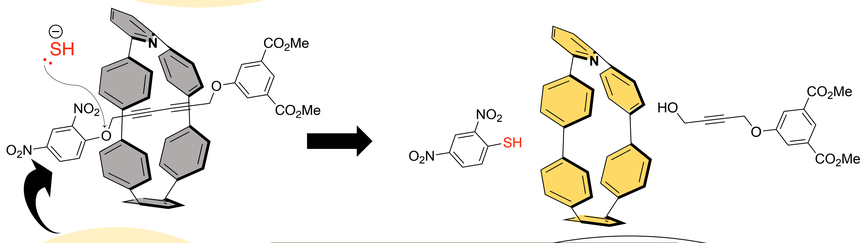
The Jasti lab is an organic synthetic lab that specializes in carbon nanohoops, or [*n*]-cycloparaphenylenes ([*n*]-CPPs) which are new nanostructures with size dependent fluorescence that can be leveraged for biological studies. In my specific project, we utilize nanohoops in mechanically interlocked molecules (MIMs) which are molecules held together by physical bonds that cannot be separated without breaking a chemical bond between atoms.

The nanohoop-based [2]-rotaxane is a sensing platform utilizing carbon nanohoops and a modular linear component to detect biologically relevant analytes.

Previous work detecting hydrogen sulfide

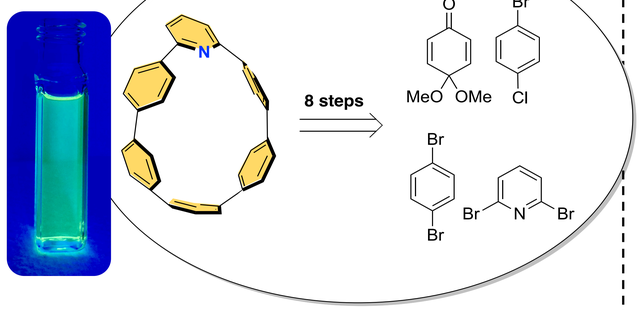
Hydrogen sulfide reacts with the structure, which prompts dethreading

This affords a turn-on fluorescence response



In the interlocked state, the rotaxane is non-fluorescent due to the 2,4-dinitrophenol stopper group that acts as a quencher

Synthesis of the mN[6]-CPP



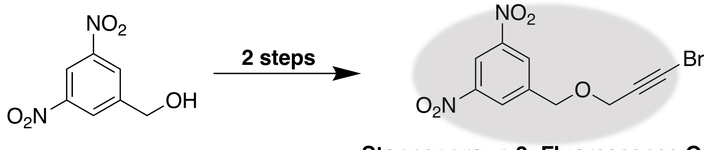
This provides a foundation for a modular sensing platform where the sensing component can be interchangeable to react with different biological analytes

Goal: Synthesize a nanohoop-based [2]-rotaxane to sense reactive oxygen species (ROS).

ROS are a source of oxidative stress, and an imbalance of ROS oxidants is connected to severe human diseases such as cancer, cardiovascular disorders, and neurodegenerative diseases.

Results

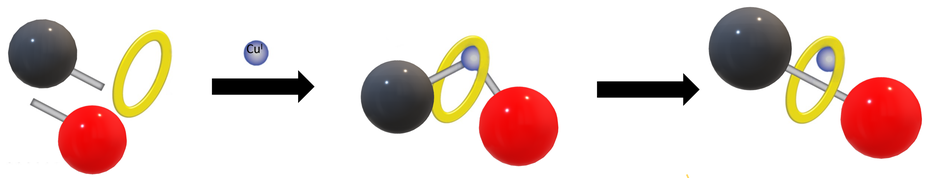
Stopper group 1: Boronate Ester Trigger



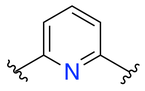
Stopper group 2: Fluorescence Quencher

Boronate ester reacts with ROS

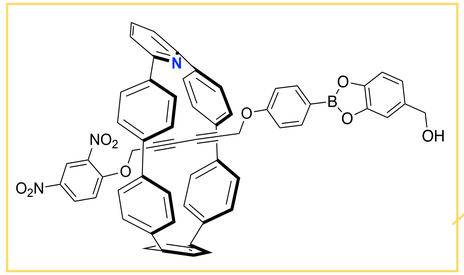
Active-Template Method



The nanohoop embedded with a 2,6-pyridyl moiety catalyzes bond formation in the interior of the nanohoop



2,6-pyridine



Future Directions

- Optimize synthesis/purification
- Characterize structure
- Introduce ROS to nanohoop rotaxane in simple non-biological environments simulating physiological conditions
- Assess its ability to operate in living cells

Success of the system is indicated by a turn-on fluorescence response to ROS

Acknowledgements

Professor Ramesh Jasti

Current members:

Ruth Maust	Tara Clayton
Claire Otteson	Luca Zocchi
Tavis Price	Phyllis Liao
James May	Anna Garrison
Julia Fehr	Eric Krall
Hannah Hashimoto	Jacob Lorenz

Sources

Otteson, Claire; Levinn, Carolyn; Van Raden, Jeff; Pluth, Michael; Jasti, Ramesh, *Nanohoop Rotaxane Design to Enhance Selectivity of Reaction Based Probes: A Proof of Principle Study.* **2020**, ChemRxiv.

Van Raden JM, White BM, Zakharov LN, Jasti R. *Nanohoop Rotaxanes from Active Metal Template Syntheses and Their Potential in Sensing Applications*. Angew Chem Int Ed Engl. **2019** May 27;58(22):7341-7345

Michelle C. Y. Chang, Arnd Pralle, Ehud Y. Isacoff, and Christopher J. Chang, *A Selective, Cell-Permeable Optical Probe for Hydrogen Peroxide in Living Cells,* Journal of the American Chemical Society **2004** 126 (47), 15392-15393

Stoddart JF. *Mechanically Interlocked Molecules (MIMs)-Molecular Shuttles, Switches, and Machines* (Nobel Lecture). Angew Chem Int Ed Engl. **2017** Sep 4;56(37):11094-11125

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