

# Total Synthesis of (+)-Lycoricidine and (+)-Narciclasine

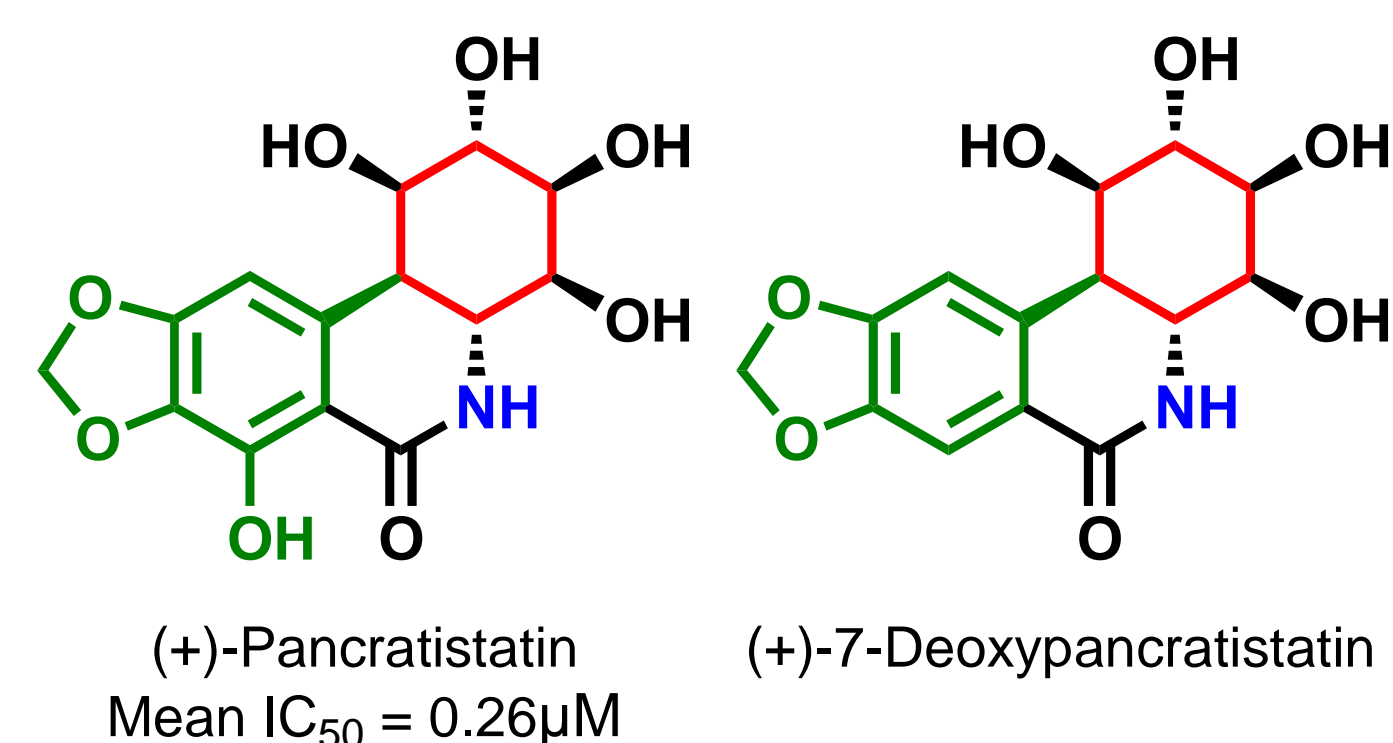
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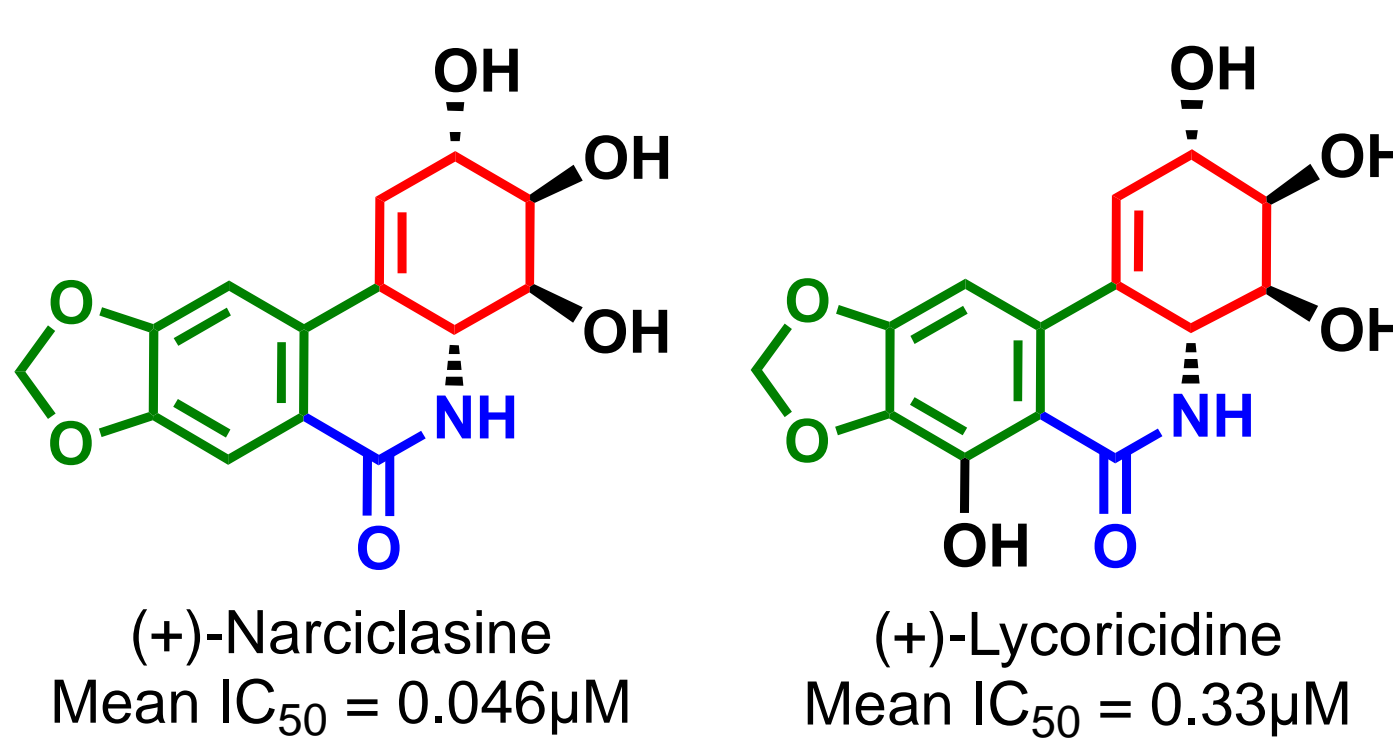
## Introduction

### Amaryllidaceae Isocarbostryl Alkaloids

Previous Work:



This Work:



### Pharmacological Properties:

- 1,2,3,4
- Antibacterial
- Antiviral
- Selective Sub- M Anticancer Cytotoxicity
- Broad Therapeutic Window

### Isolation Yields:

- 1,2,3,4
- (+)-Pancratistatin: 125 mg/kg
- (+)-Lycoricidine: 222mg/kg
- (+)-Narciclasine: 135 mg/kg
- (+)-7-Deoxypancratistatin: 3 mg/kg

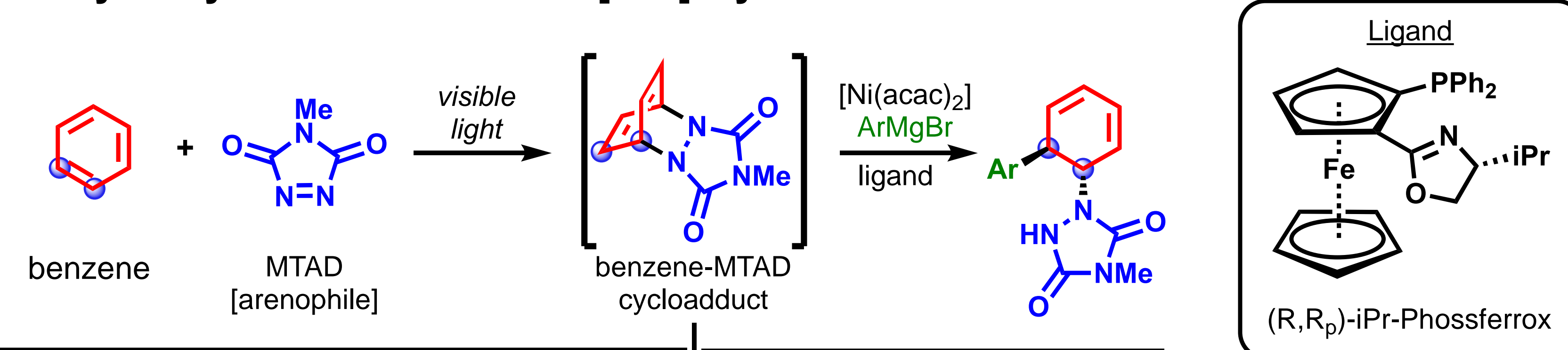
\*All yields decreased when the plants were cultivated

### Synthetic Challenges:

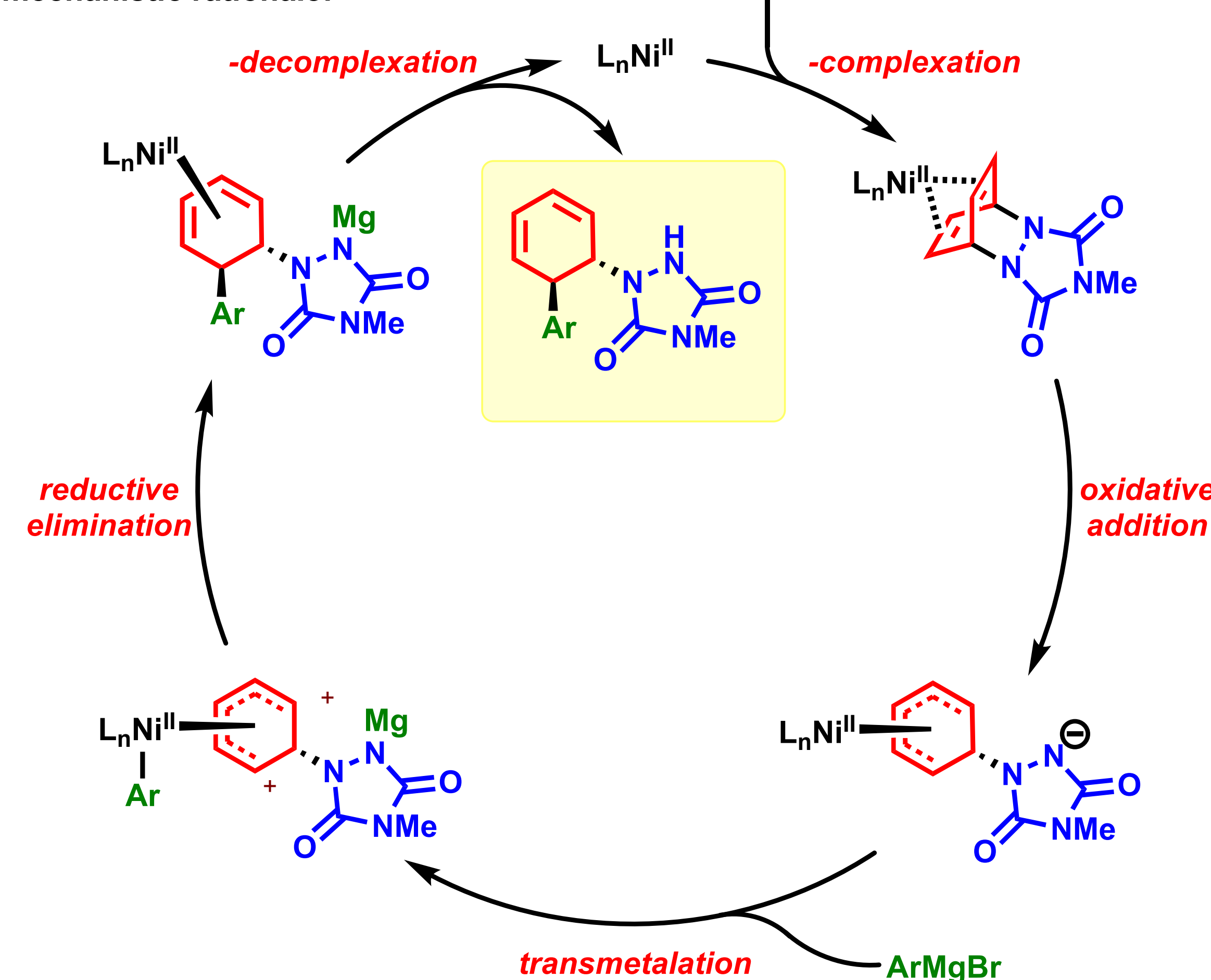
- Highly functionalized
- Four or six contiguous stereocenters

## Methodology

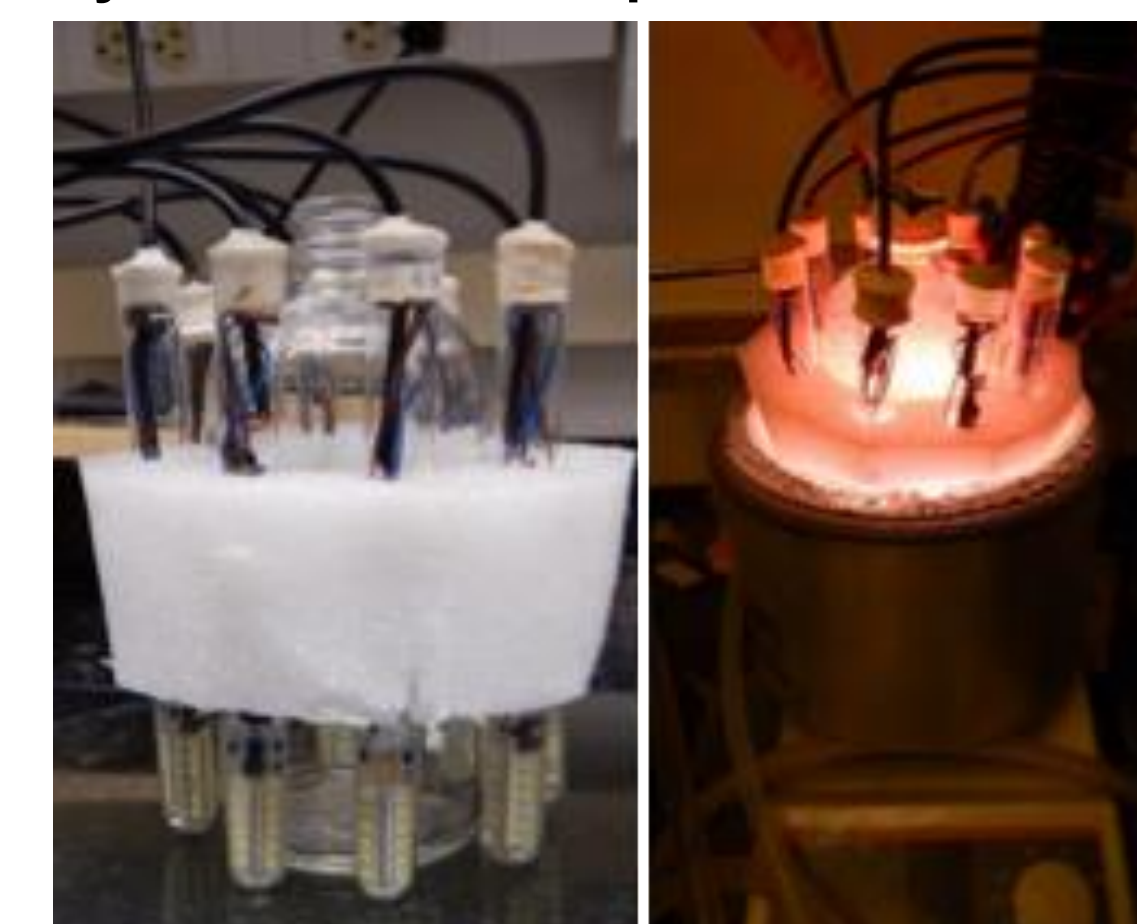
### Catalytic Cycle of Dearomative [4+2]-Cycloaddition<sup>5</sup>



mechanistic rationale:

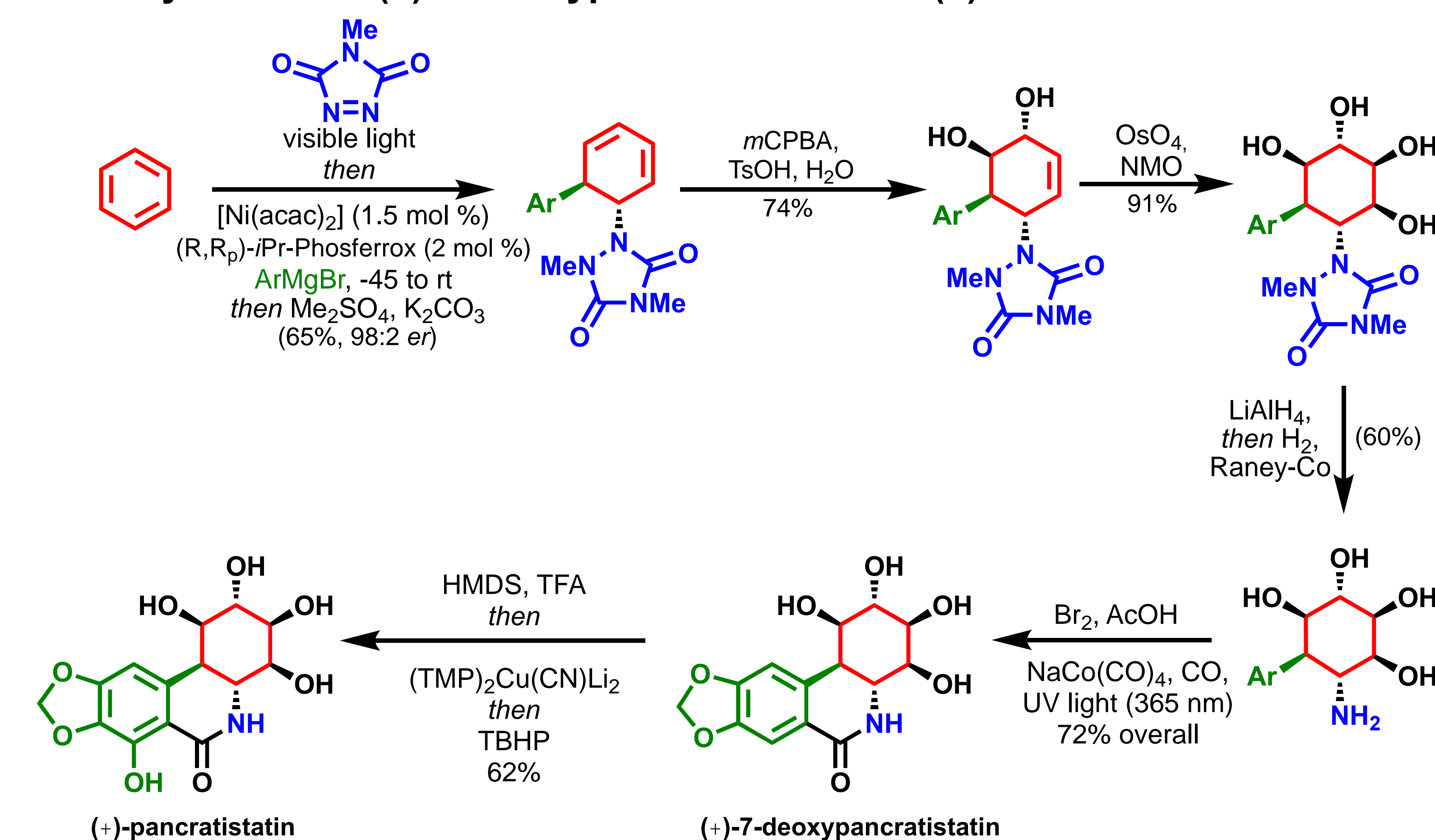


Cycloaddition Set-Up:



## Previous Work

### Total Synthesis of (+)-7-Deoxypancratistatin and (+)-Pancratistatin<sup>5</sup>



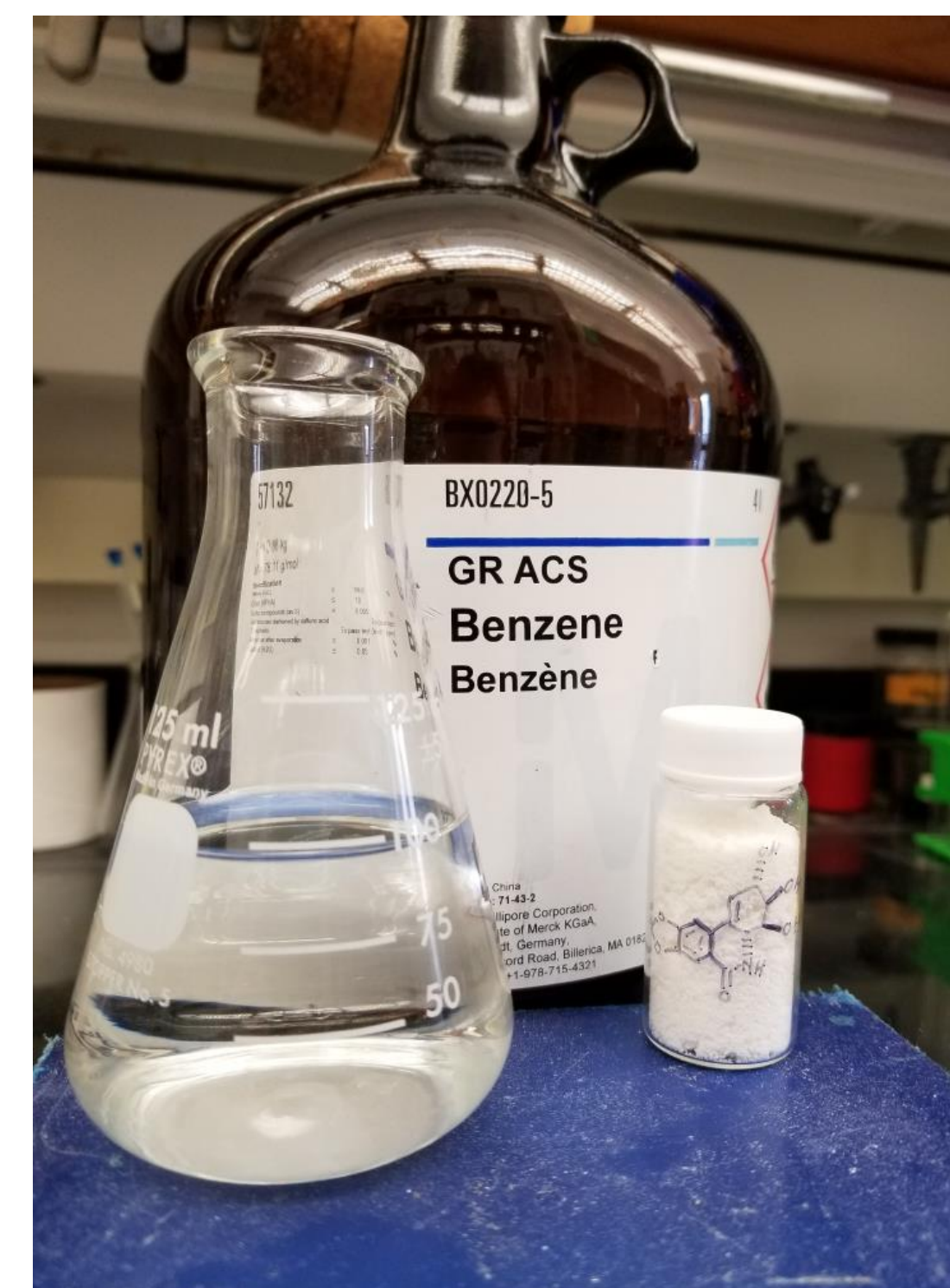
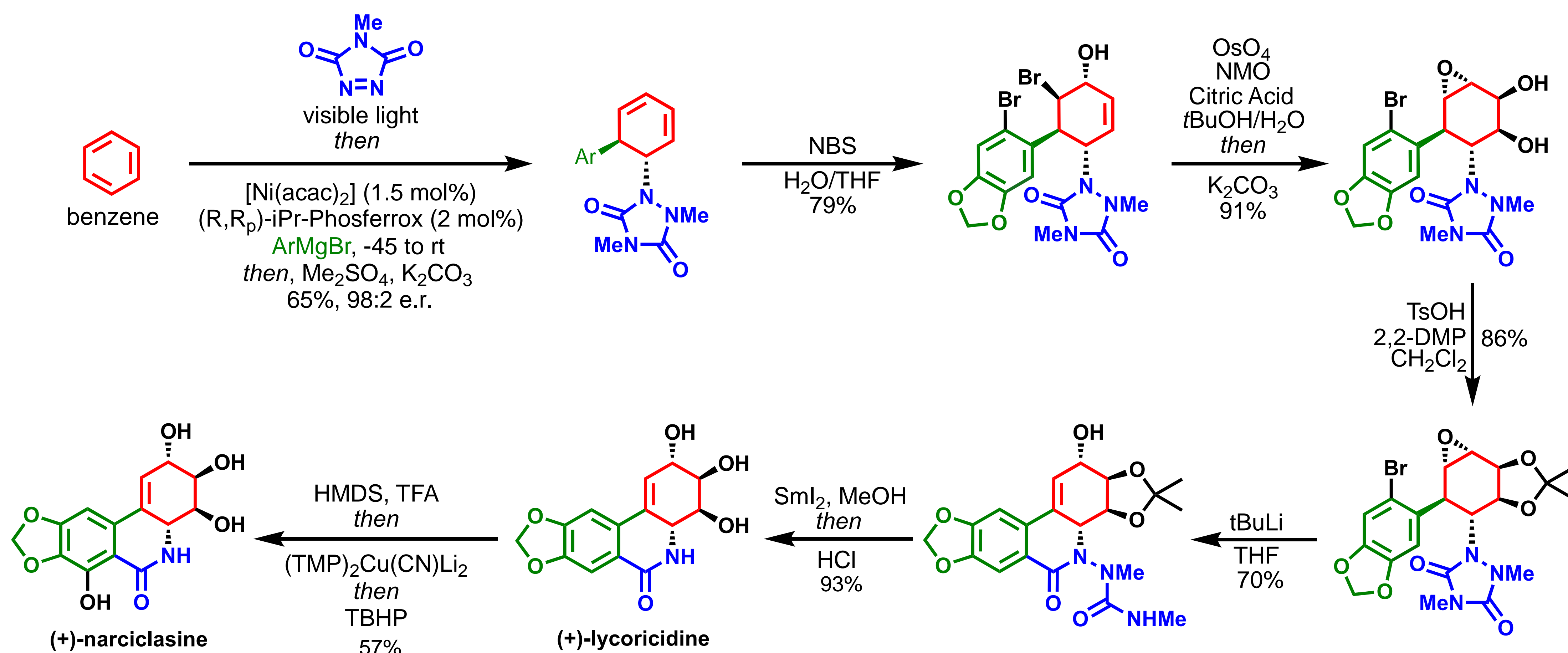
## Results

- (+)-Pancratistatin: 200 mg isolated, 12% overall yield
- (+)-7-Deoxypancratistatin: 1.6 g isolated, 19% overall yield
- (+)-Narciclasine: 1.8 g isolated, 15% overall yield
- (+)-Lycoricidine: > 8.1 g isolated, 26% overall yield

- Syntheses starts from benzene, a feedstock solvent
- Scalable routes provide material for further biological studies
- Modular synthesis allows for rapid access to analogues

## Current Work

### Total Synthesis of (+)-Narciclasine and (+)-Lycoricidine



8.1 grams of (+)-lycoricidine from 100 ml of benzene



### Acknowledgments:

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### References:

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- 2.) *Apop.*, **2005**, 10 (3), 619
- 3.) *Transl. Oncol.*, **2008**, 1 (1), 1
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