Toward the synthesis of an acetal-free Tn antigen anti-cancer vaccine candidate

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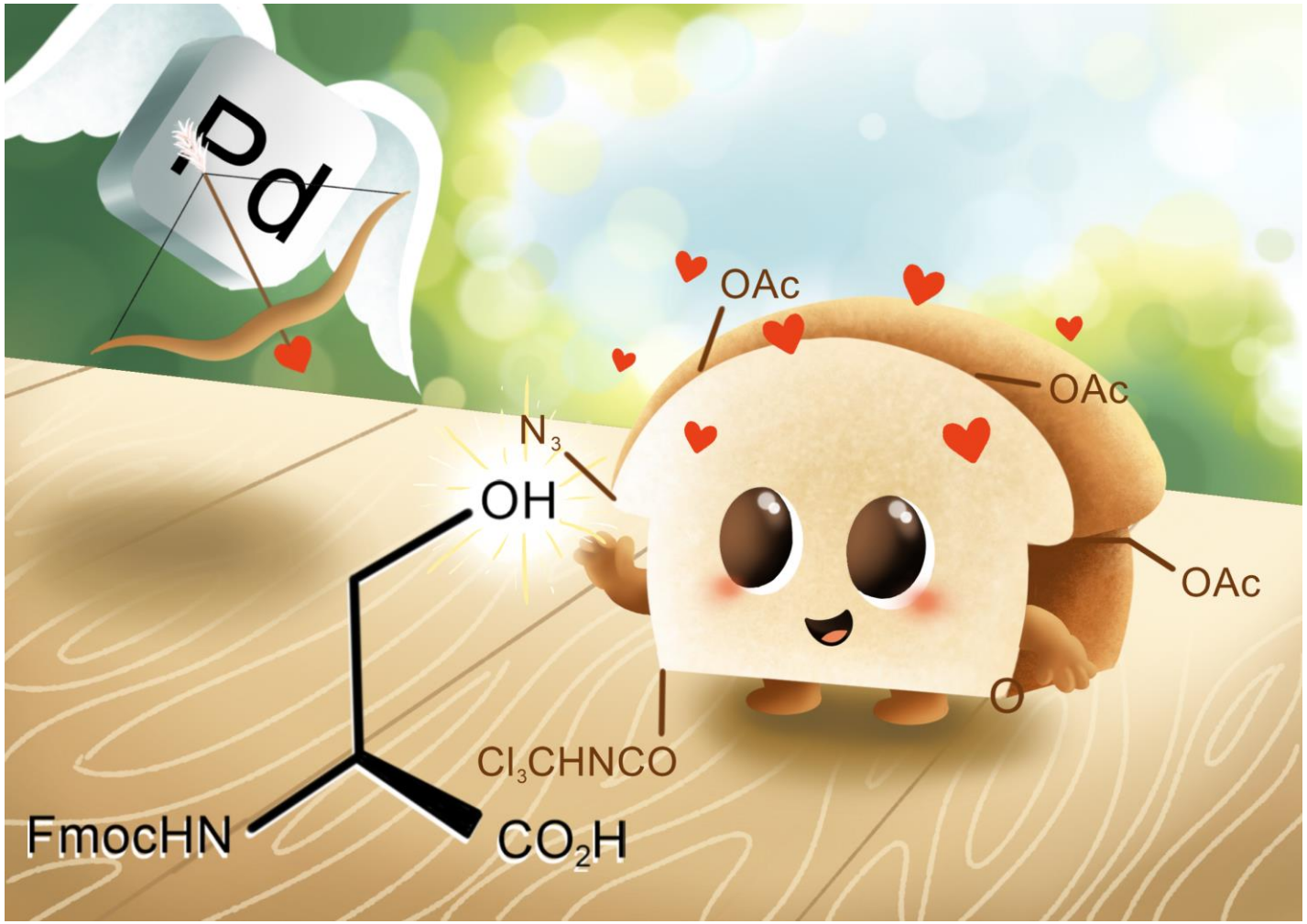

Toward the Synthesis of an Acetal-free Tn Antigen Anti-Cancer Vaccine Candidate

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University of Windsor

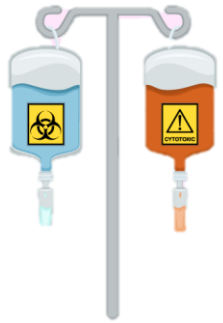
Presented: ***March 2022***

Presenter: ***Chelsea Ymana***

Supervisor: ***Dr. John F. Trant***

A Direction Towards Cancer Treatment

- Current treatments: Surgery, radiation, and chemotherapy



A Direction Towards Cancer Treatment

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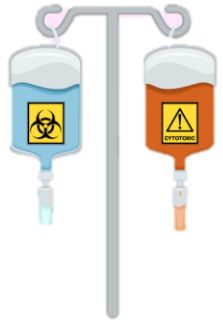
- Cancer vaccines would provide a method of activating the immune system towards cancer cells

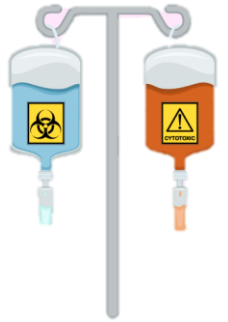


A Direction Towards Cancer Treatment

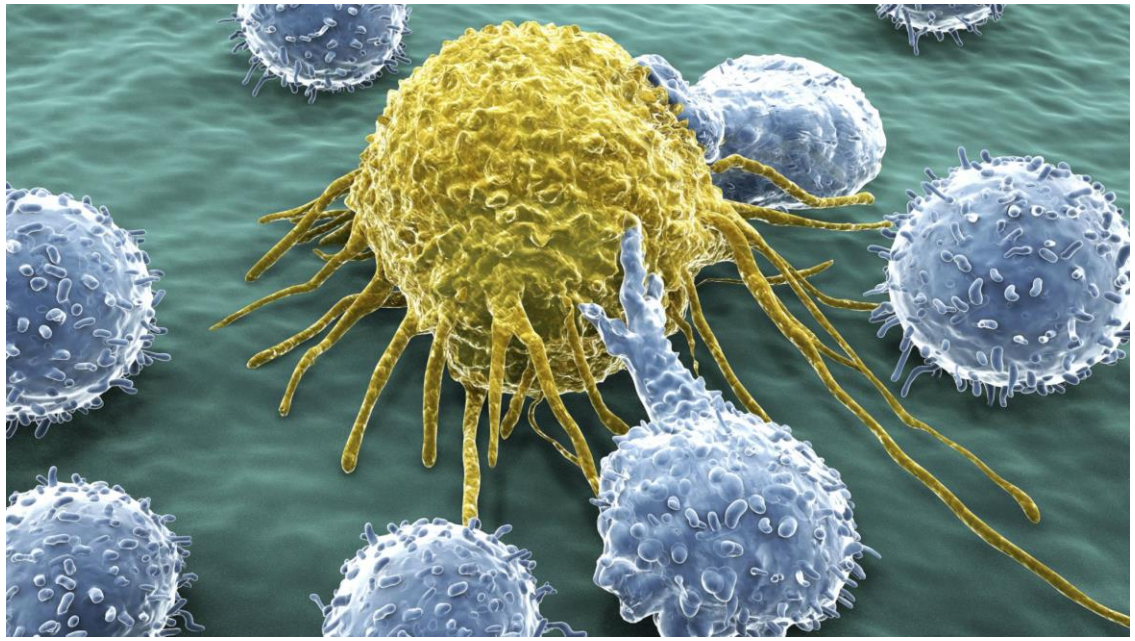
- Current treatments: Surgery, radiation, and chemotherapy

- Cancer vaccines would provide a method of activating the immune system towards cancer cells

- The challenge:
  - Many biomarkers are present on healthy cells
  - Result in autoimmune responses

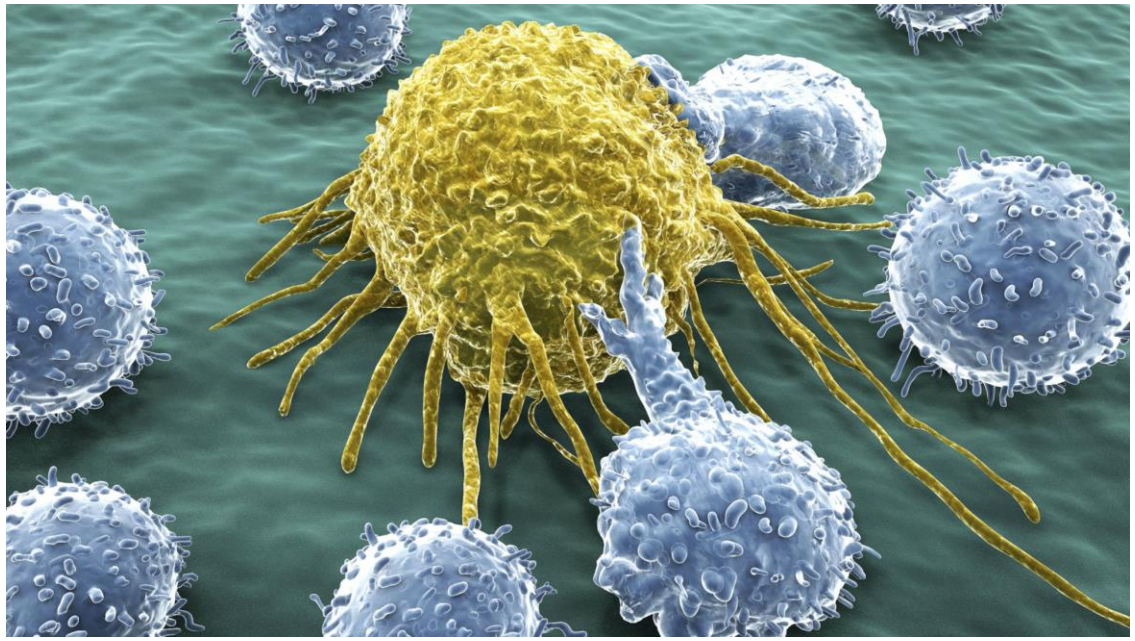


TACAs – Tumor Associated Carbohydrate Antigens

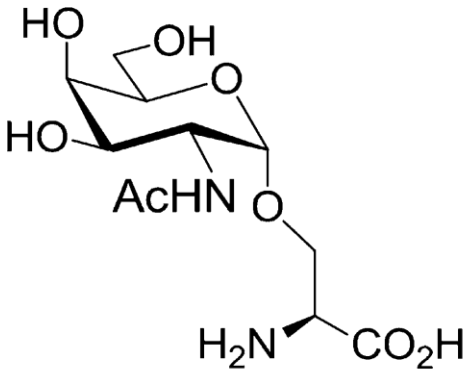


TACAs – Tumor Associated Carbohydrate Antigens

- Biomarkers found on cancer cells
- Absent from healthy adult cells
- Possible vaccine target for immunotherapy
- Our specific target: ***Tn Antigen***

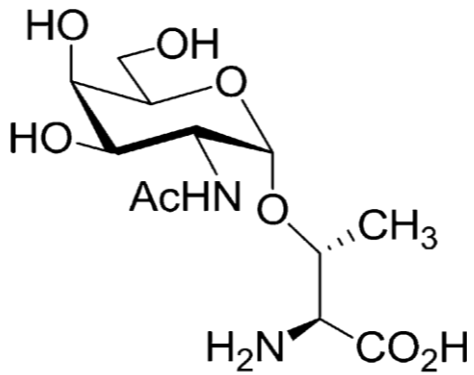


Chemical Structure of the Natural Tn Antigen



1a

Serine Derivative



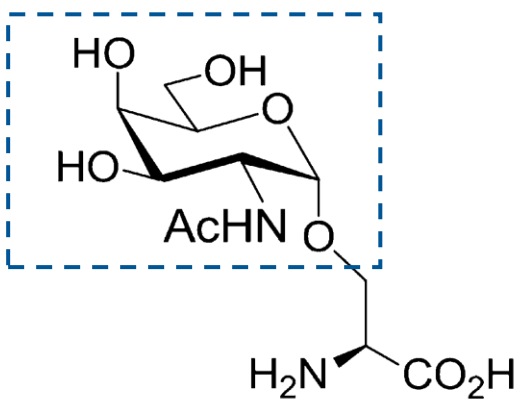
1b

Threonine Derivative

Sadraei, S. I.; Reynolds, M. R.; Trant, J. F. *Advances in Carbohydrate Chemistry and Biochemistry* **2017**, 144.

Chemical Structure of the Natural Tn Antigen

GalNac



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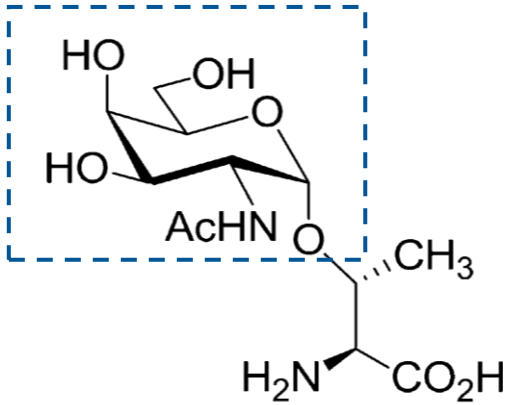

1b

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Chemical Structure of the Natural Tn Antigen

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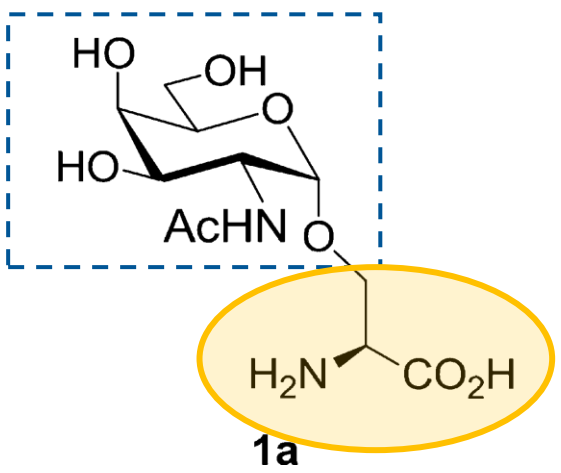

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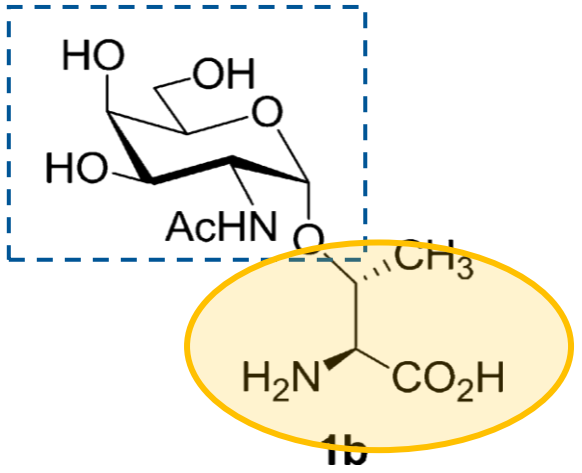

1b

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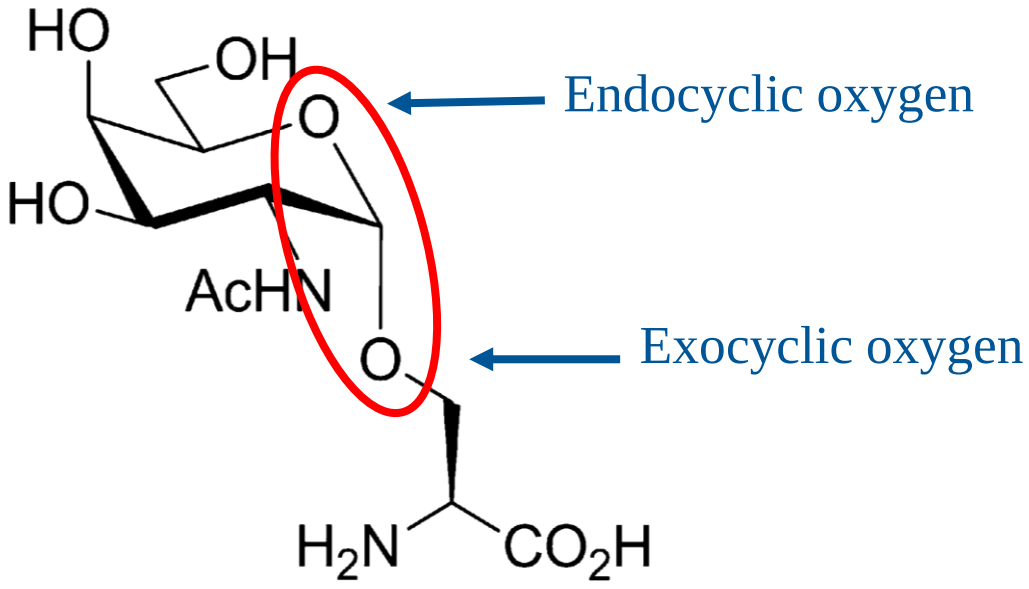
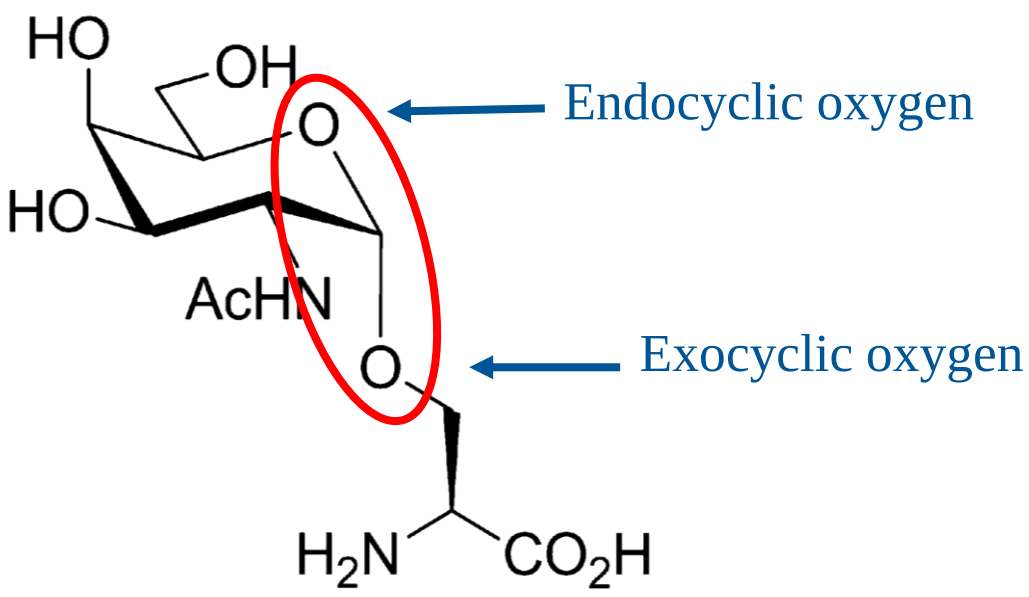
Challenge of Using the Natural Tn Antigen

Challenge of Using the Natural Tn Antigen

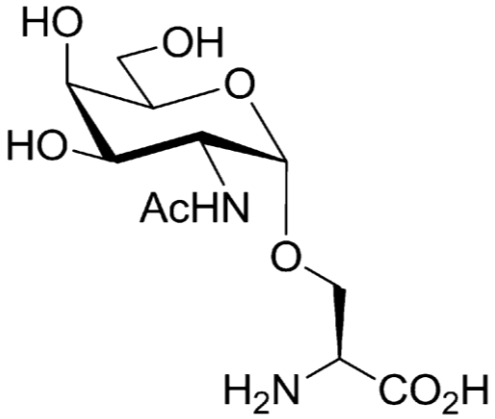


Challenge of Using the Natural Tn Antigen

- Glycosidic bond susceptible to hydrolysis by glycosidases
- Carbohydrates have a short physiological half life
- Monomers not processed by immune system



Solution: Acetal-Free Carbohydrates



O-Glycoside Tn antigen

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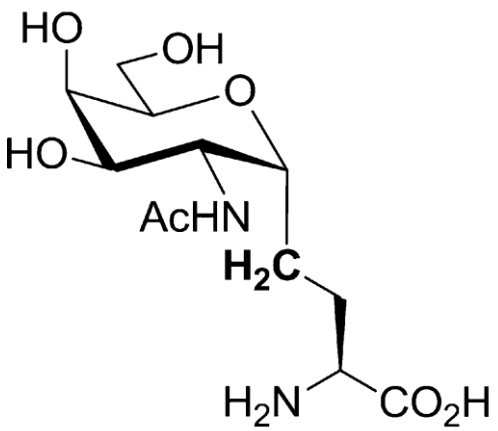
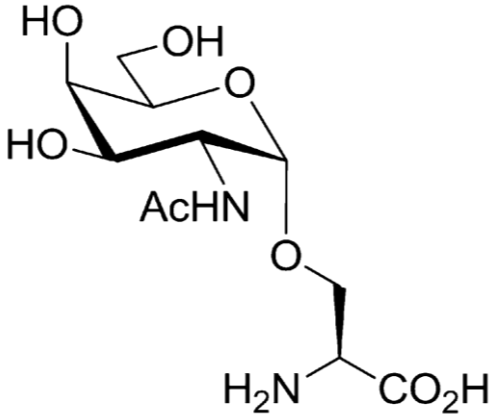
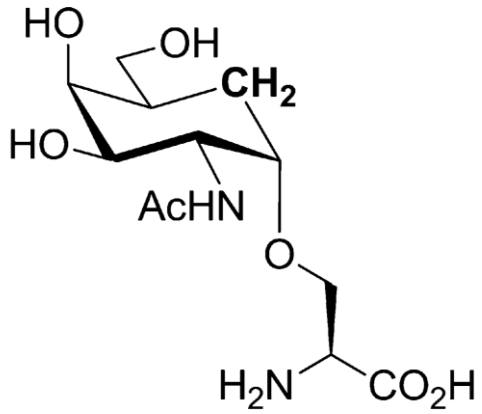
Solution: Acetal-Free Carbohydrates



C-glycoside Tn antigen



O-Glycoside Tn antigen



Carbasugar Tn antigen

Sadraei, S. I.; Reynolds, M. R.; Trant, J. F. *Advances in Carbohydrate Chemistry and Biochemistry* **2017**, 144.

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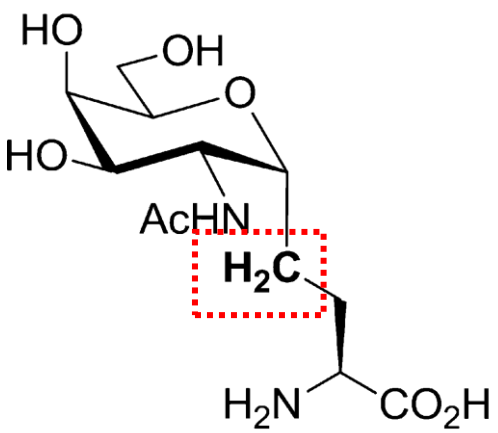

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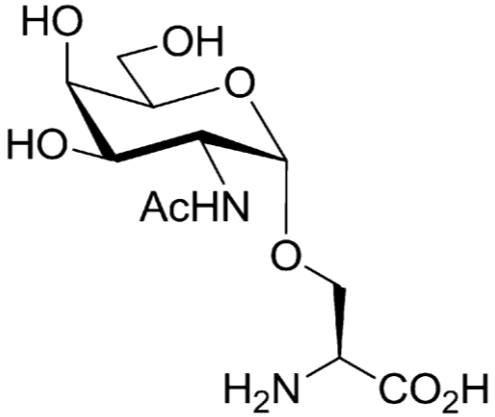

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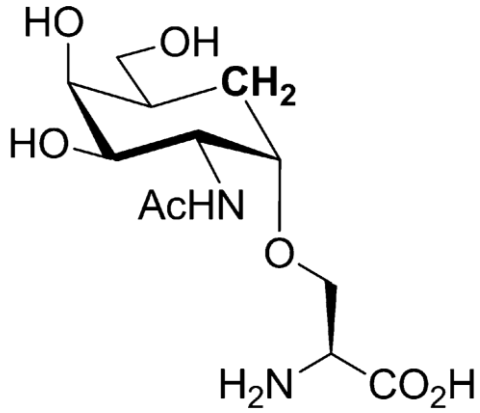

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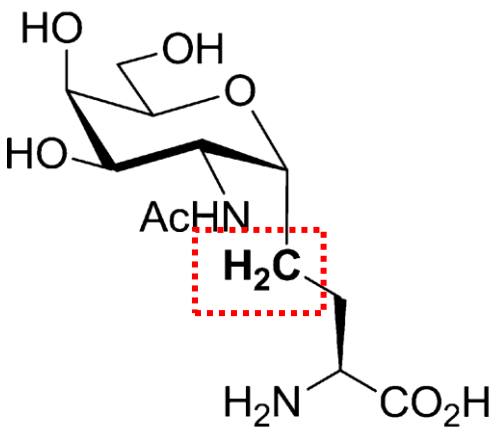

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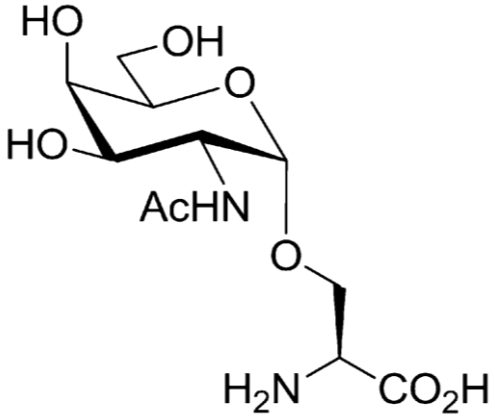

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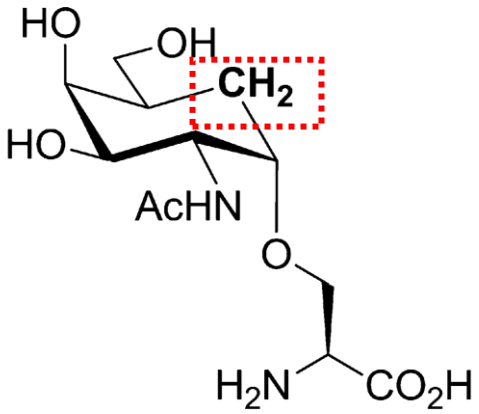
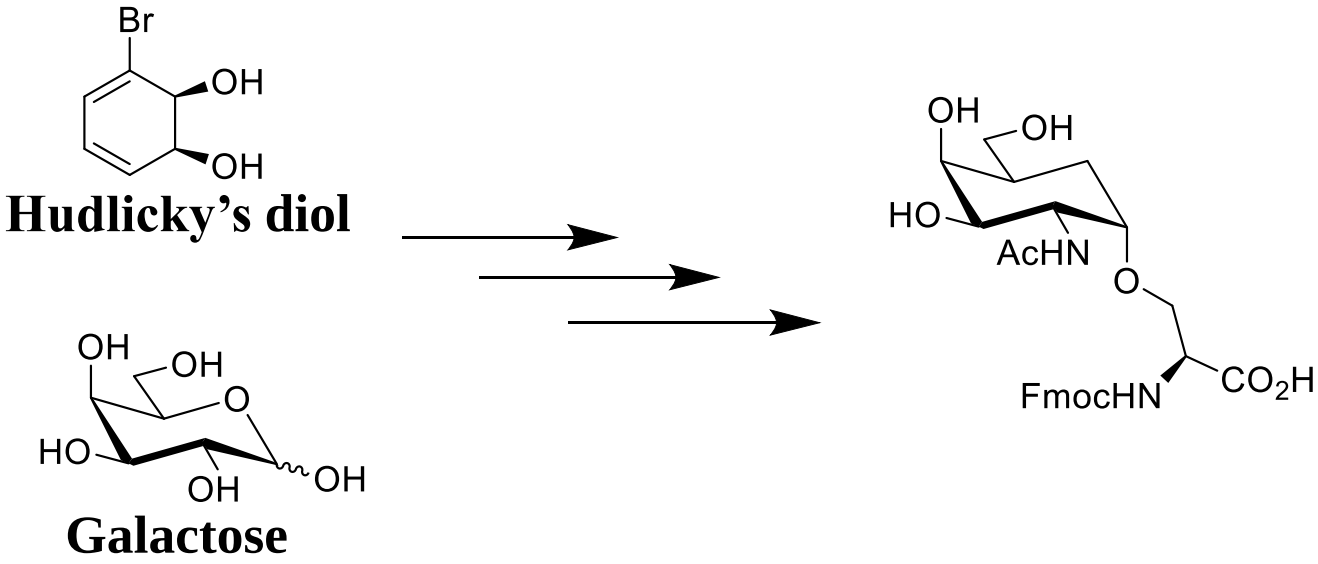


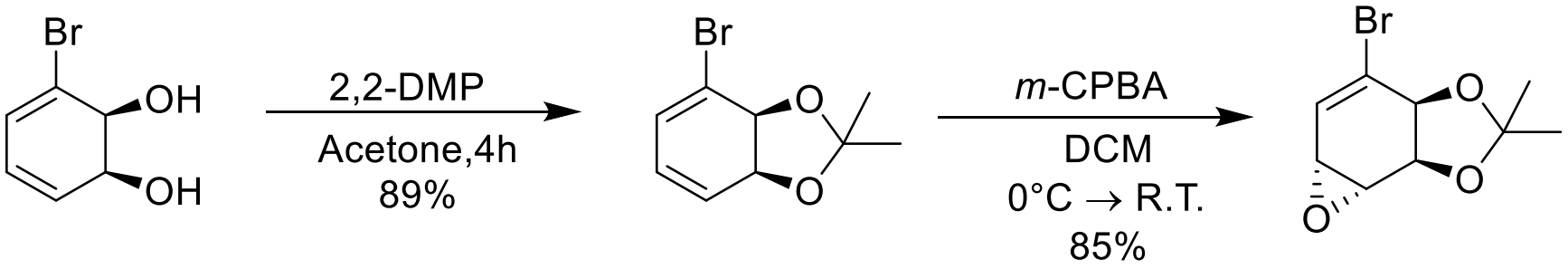
Carbasugar Tn antigen

Bilinear Synthetic Approach

- Two Possible Approaches:
  1. *De novo* synthesis
  2. Carbohydrate rearrangement



First Approach: *De Novo* Synthesis



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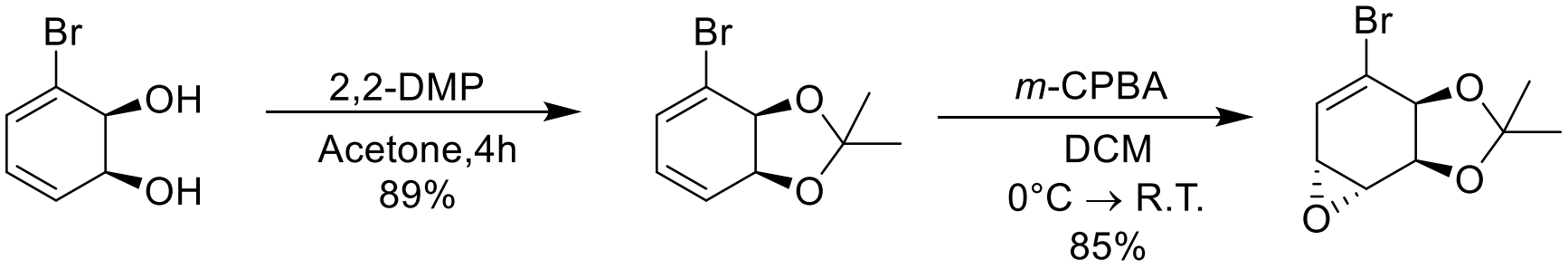
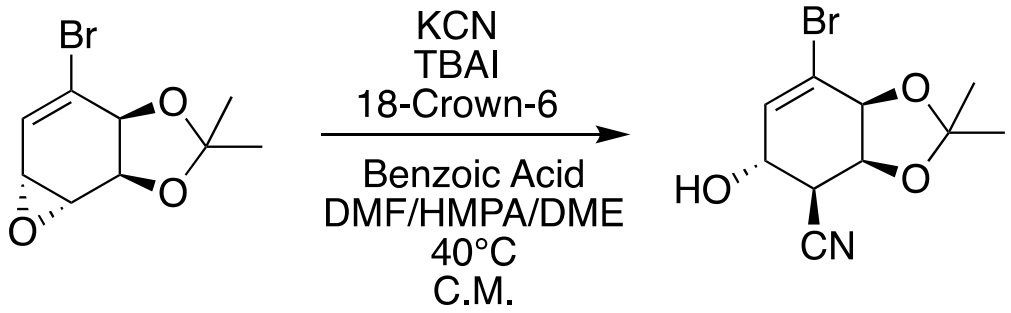


Ring opening attempt 1:



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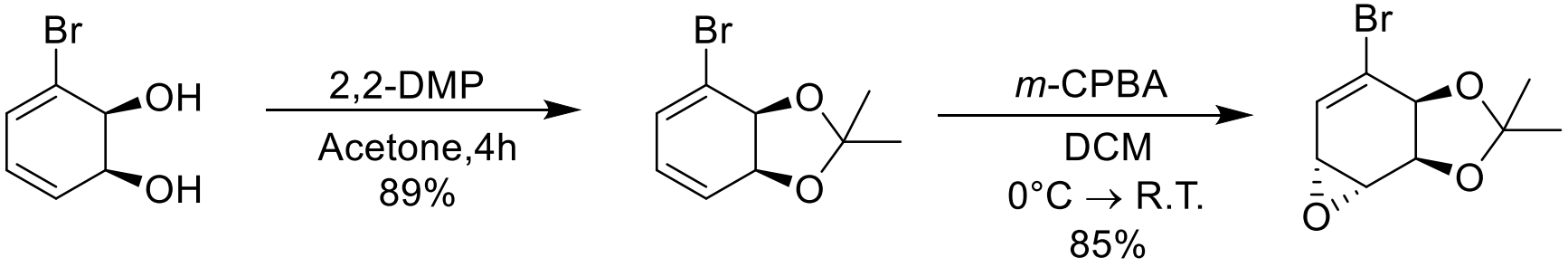

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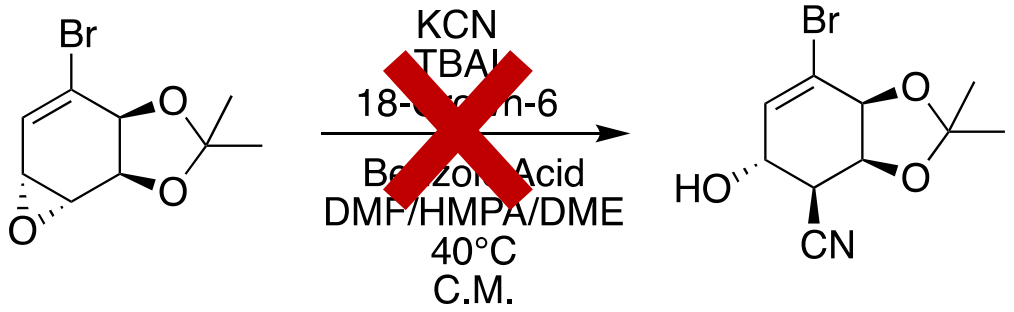

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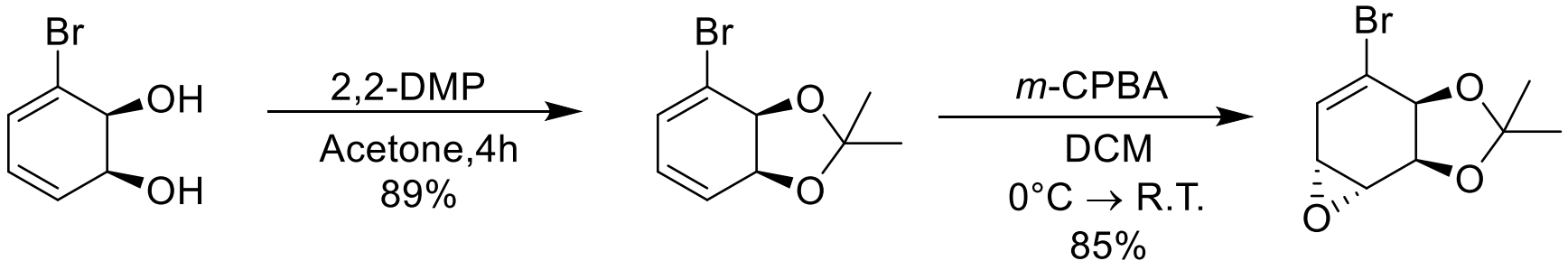
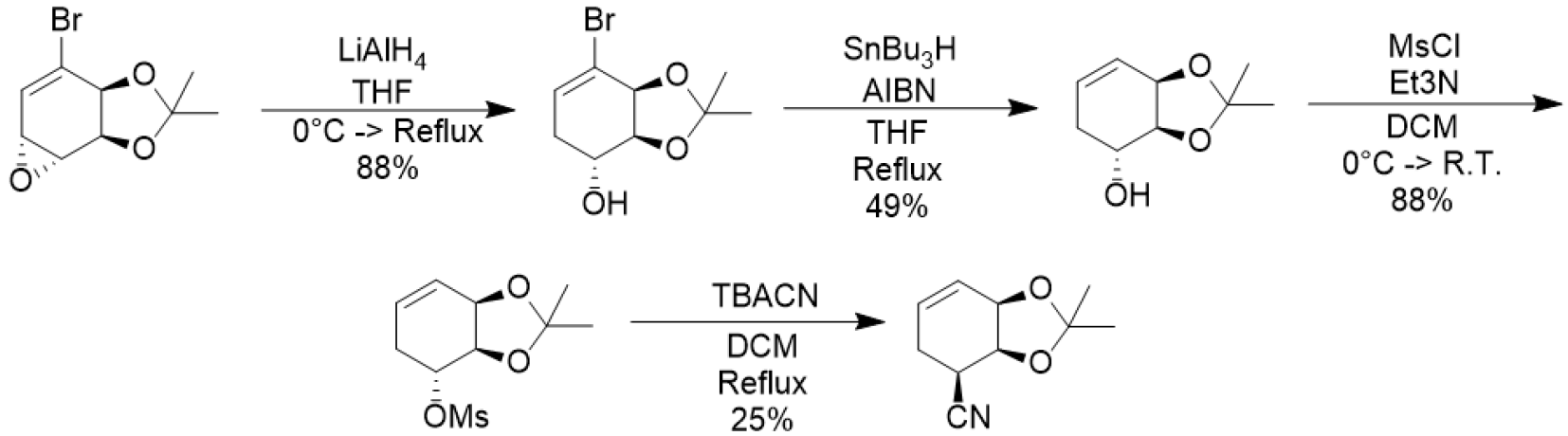


Ring opening attempt 2:



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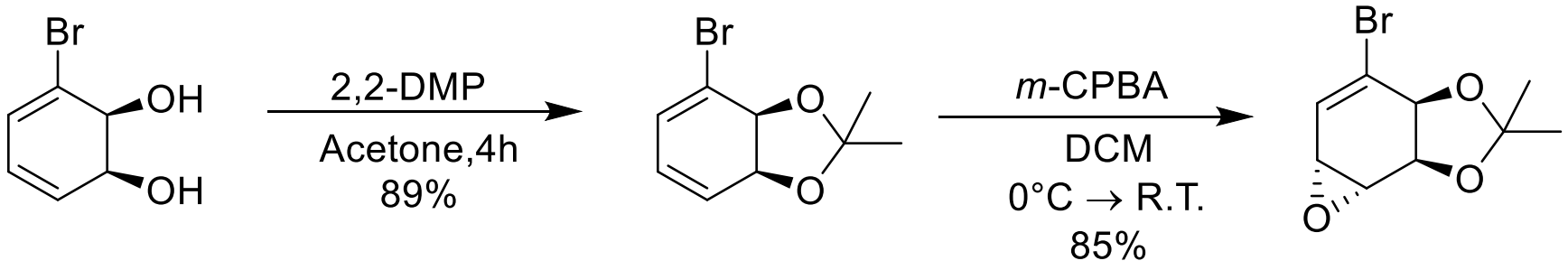

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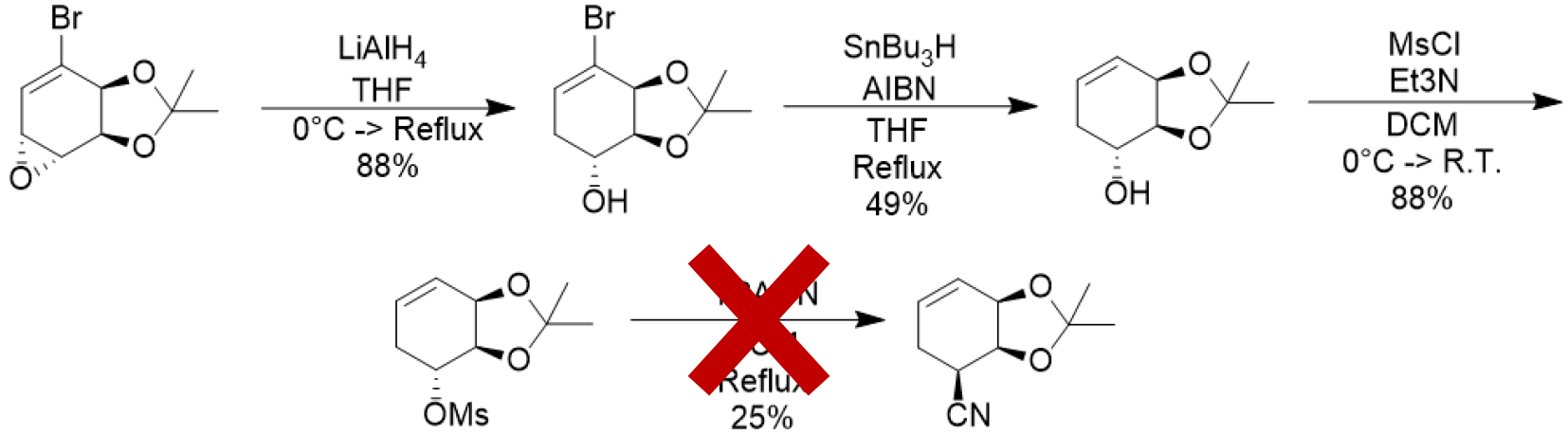
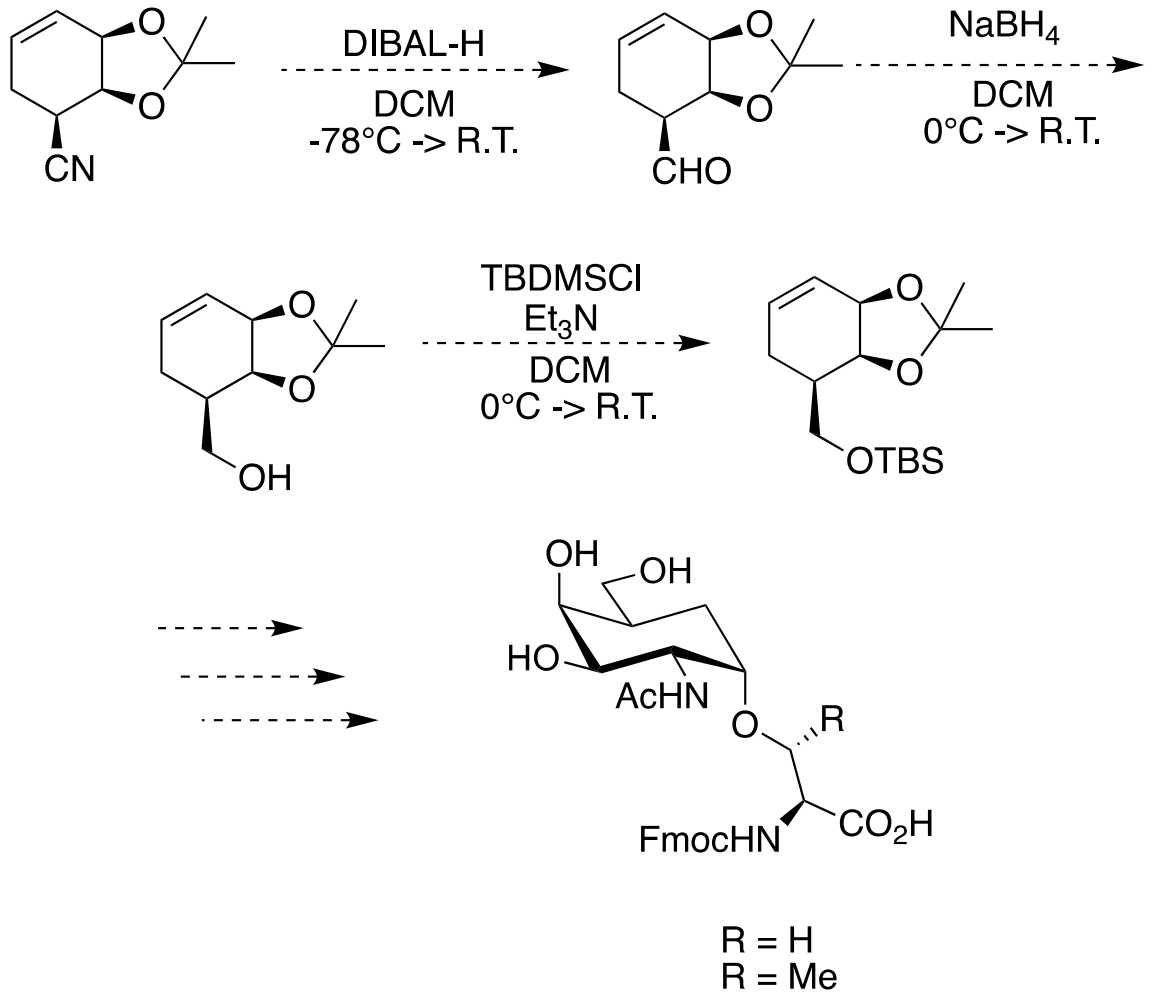
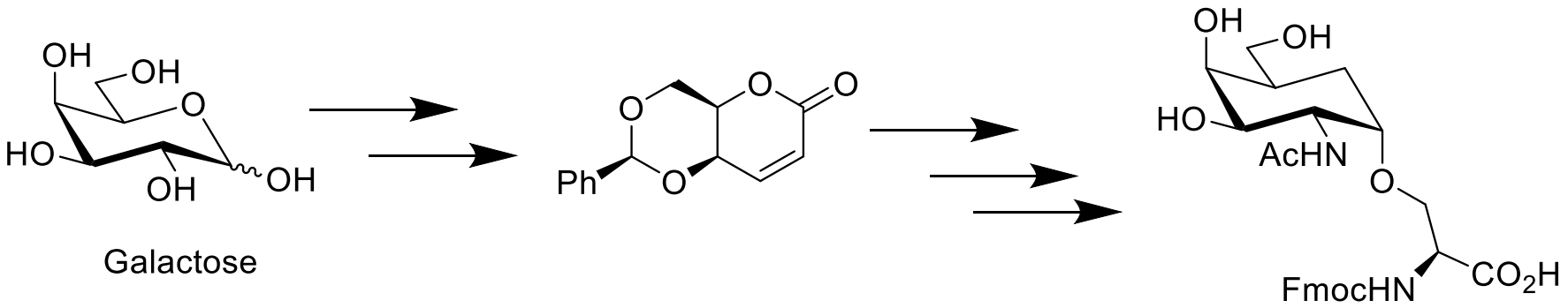


First Approach: *De Novo* Synthesis

Proposed future steps:



Second Approach: Galactose Rearrangement



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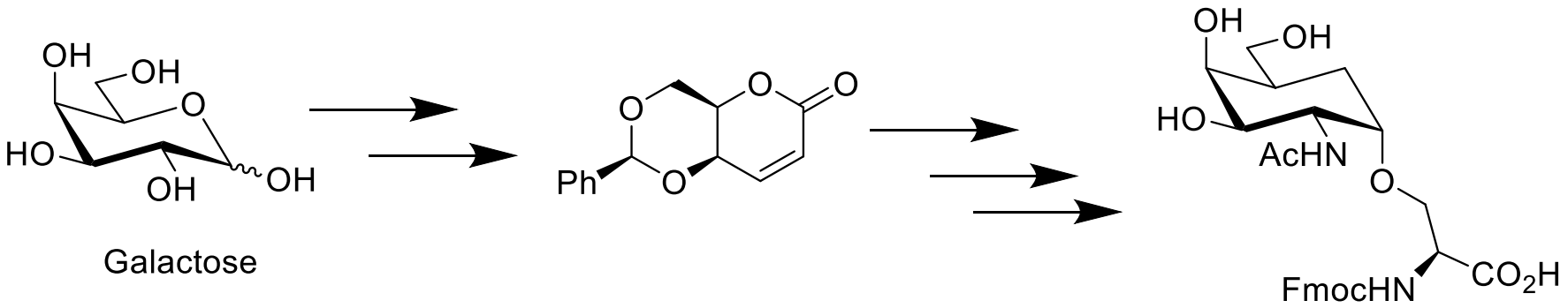

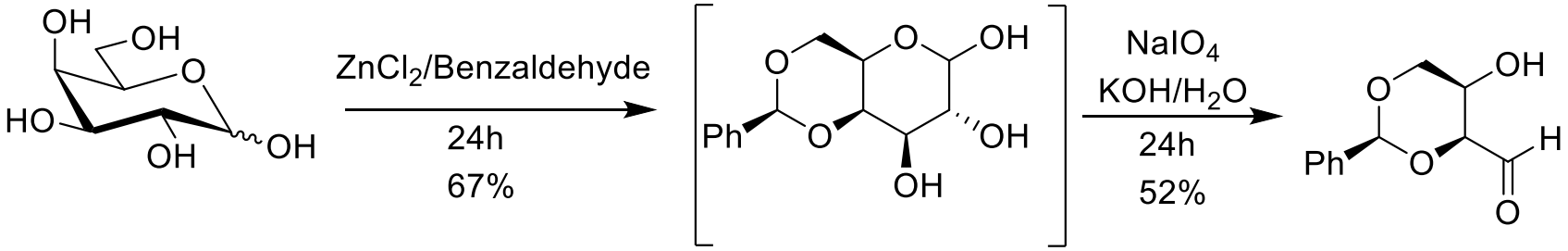

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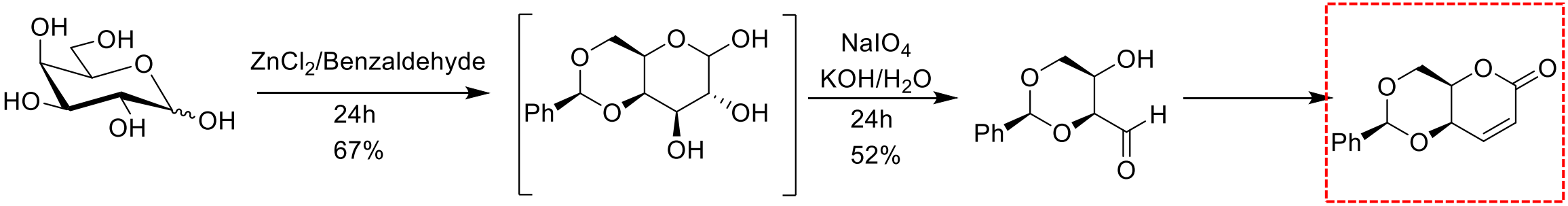

B. E. Stephens; F. Liu. *Tetrahedron Letters* 48 (**2007),** 9116–9119

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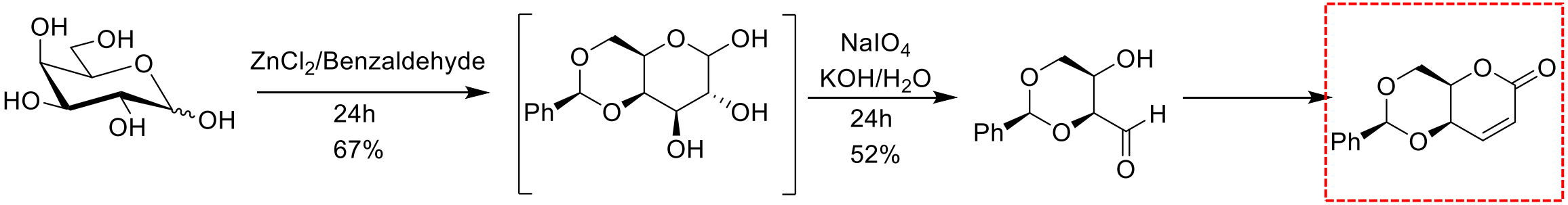
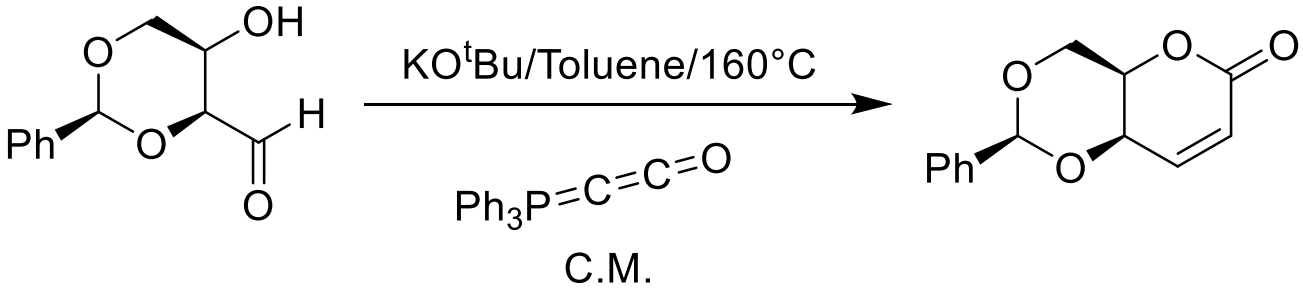


Attempt 1 to lactenone:



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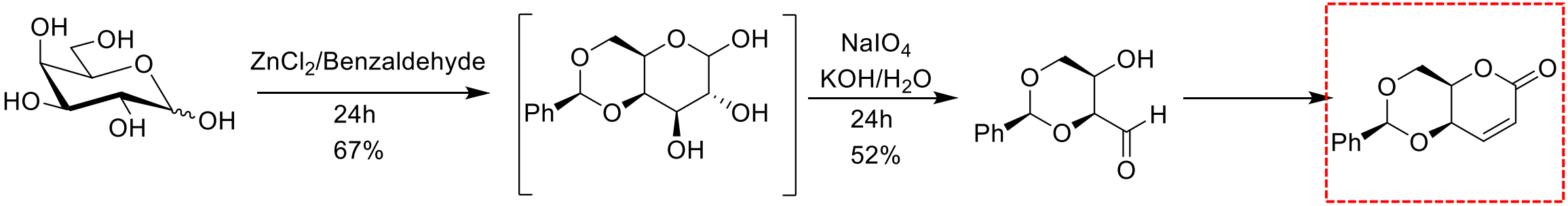
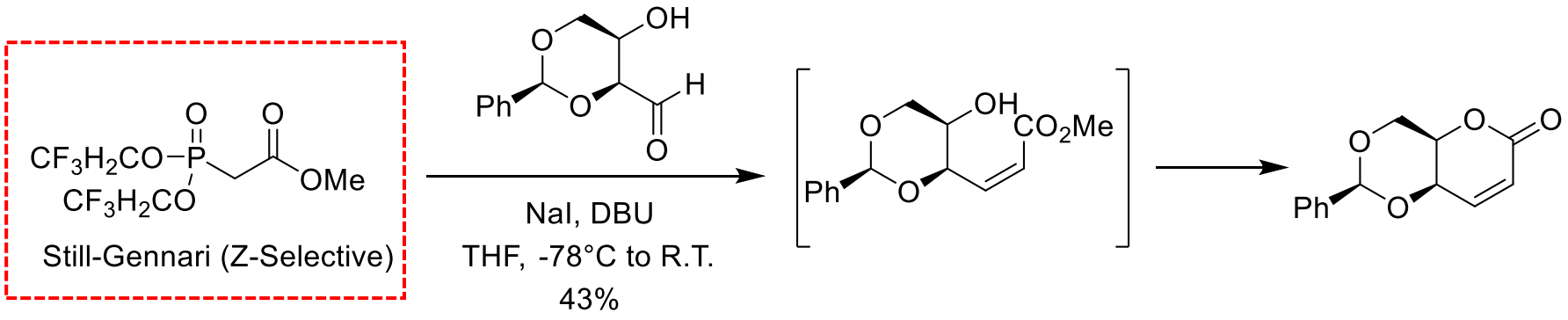


Attempt 2 to lactenone:



B. E. Stephens; F. Liu. *Tetrahedron Letters* **2007,** 48, 9116–9119, Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408

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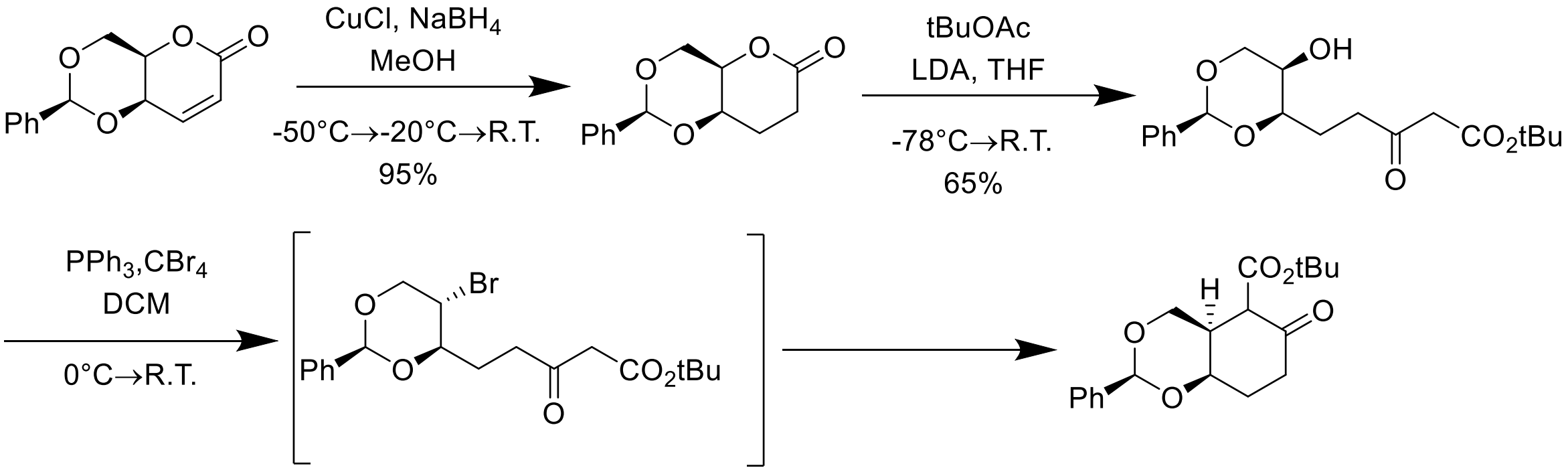
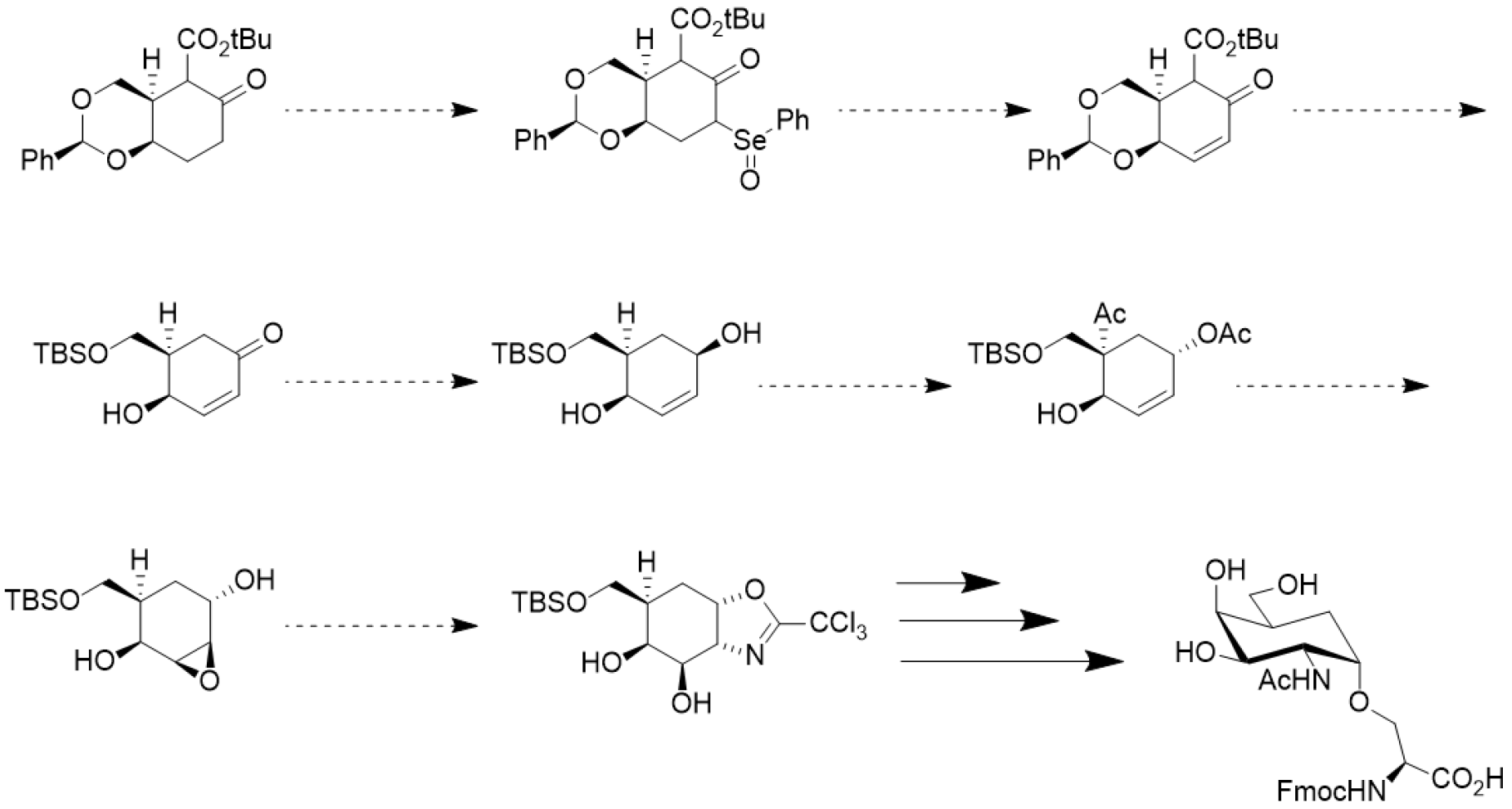


Future Synthesis

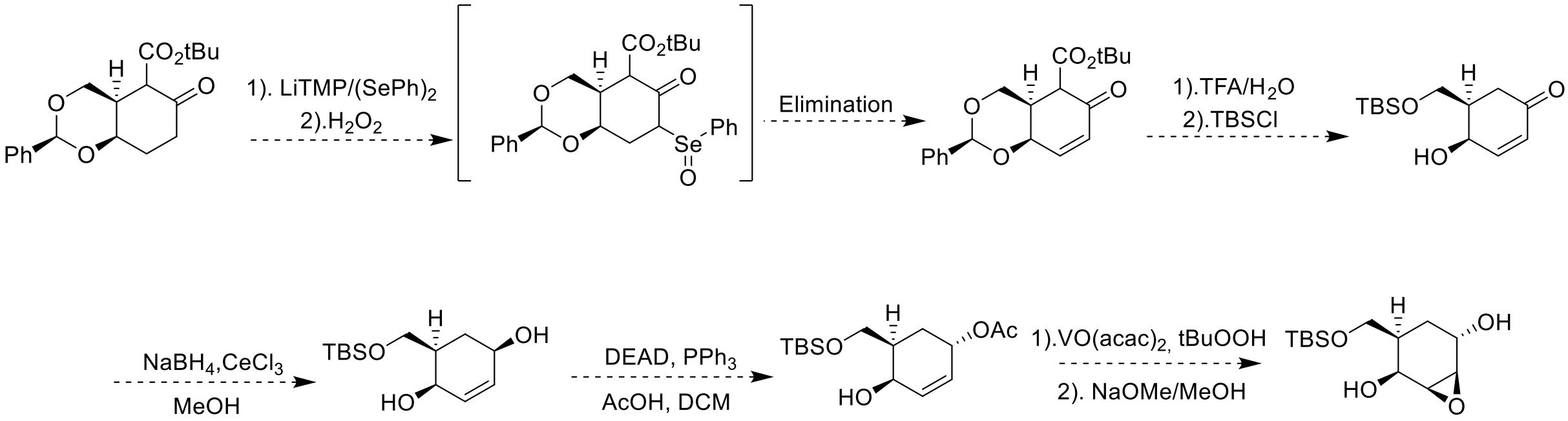


Thank you!

Supervisor: ***Dr. John F. Trant***

Mentors: ***Michael Reynolds and Dr. John J. Hayward***

Future Synthesis



Future Synthesis