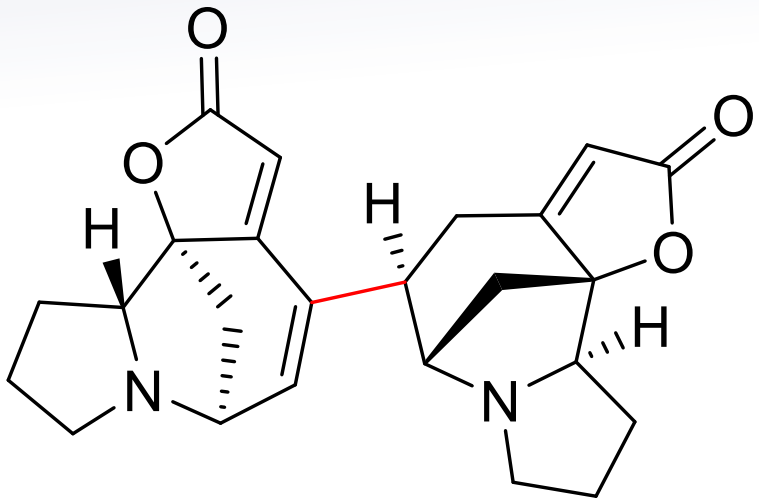
Synthesis of the Securinega Alkaloids

An Accelerated Intermolecular Rauhut−Currier Reaction Enables the Total Synthesis of (−)-Flueggenine C

Sangbin Jeon and Sunkyu Han



UNIVERSITY OF PITTSBURGH

The DIETRICH School of Arts & Sciences

Austin C. Durham

Current Literature

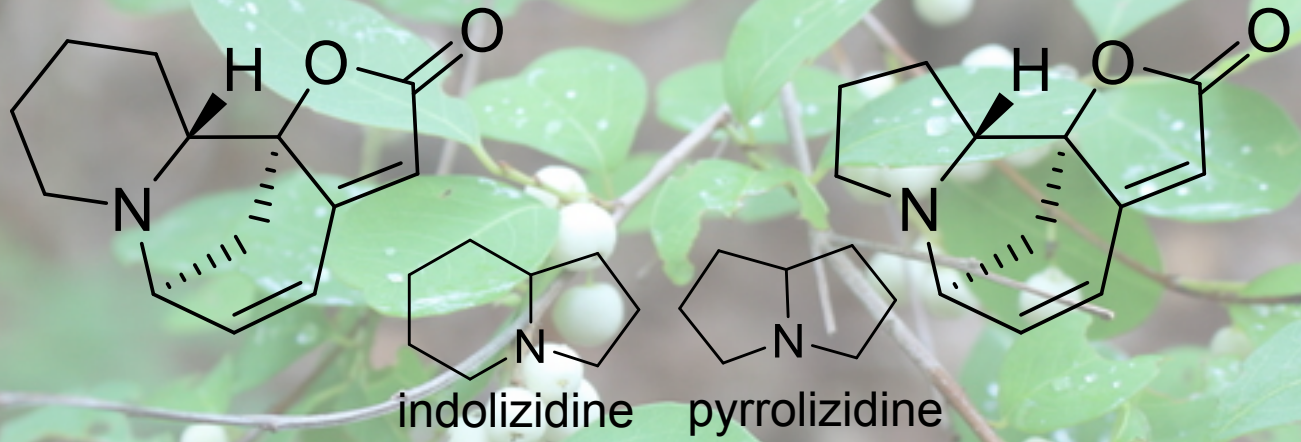
June 24th, 2017

Overview

1. The Securinega Alkaloids
2. The Rauhut-Currier Reaction
3. Total Synthesis of Flueggenine C

The Securinega Alkaloids

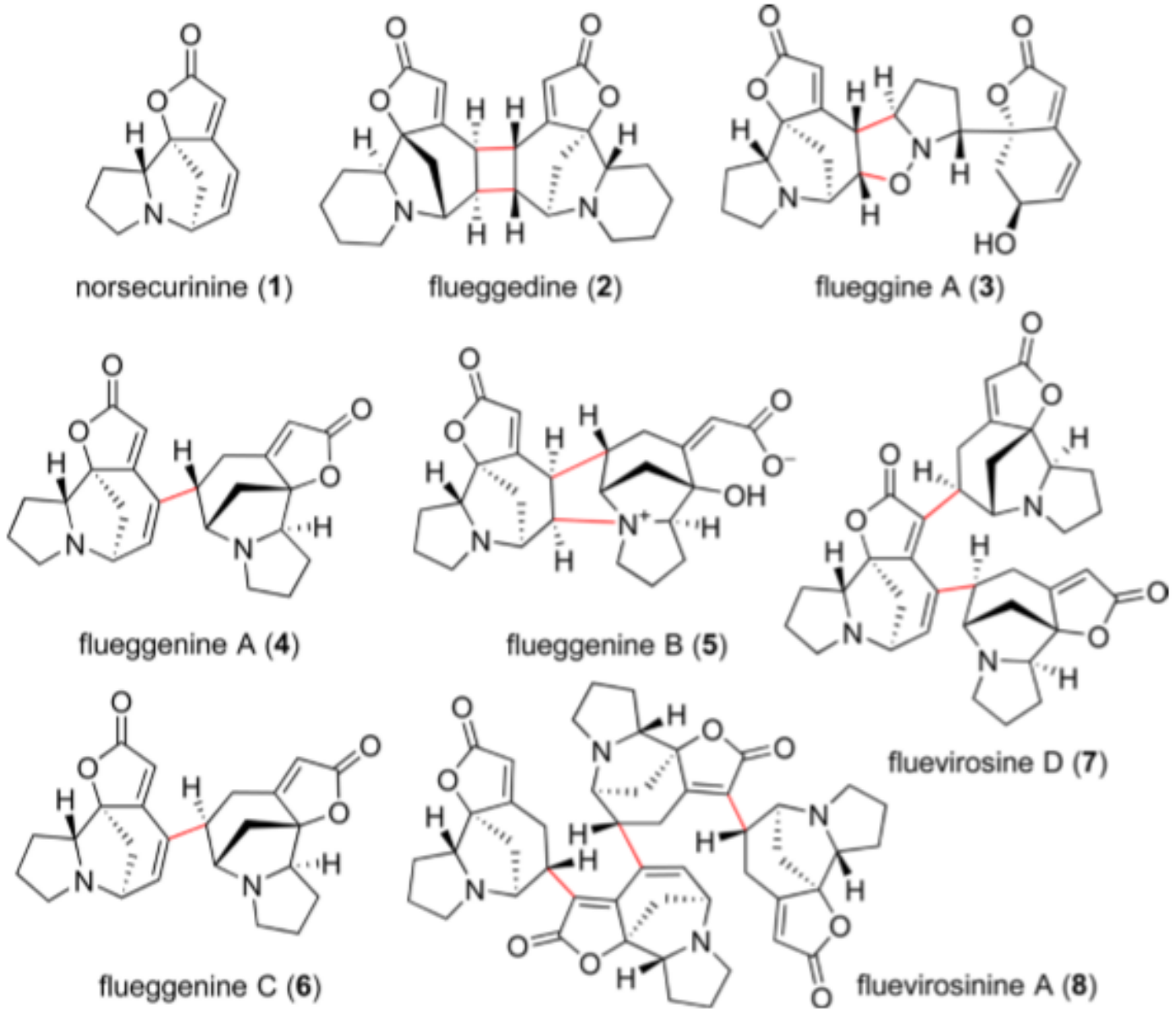
- Securinine (1956) and Norsecurinine



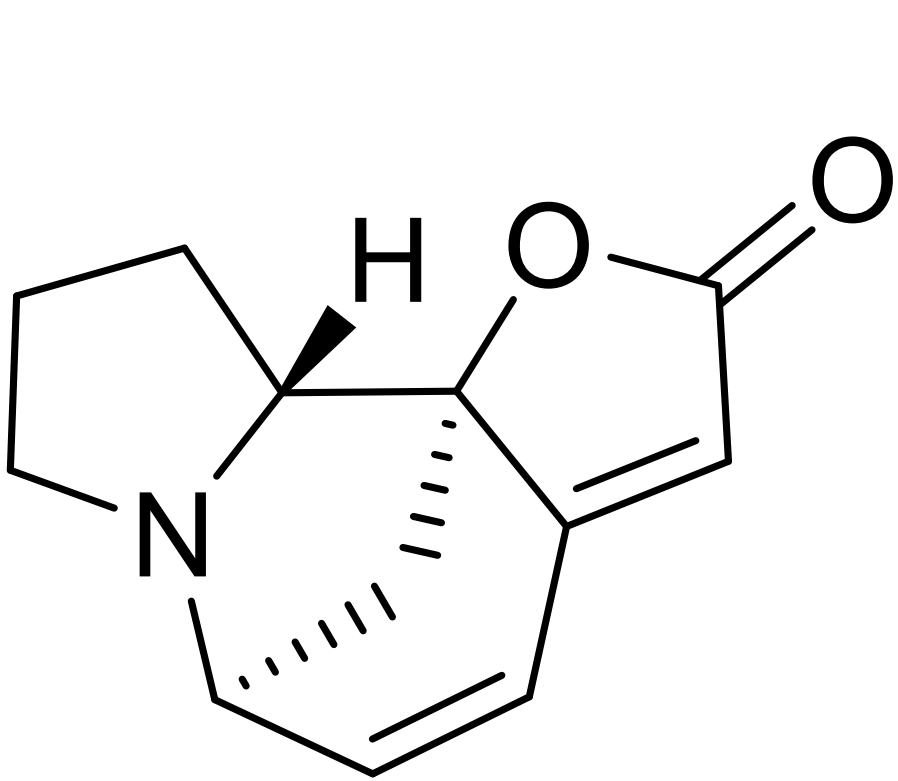
indolizidine pyrrolizidine

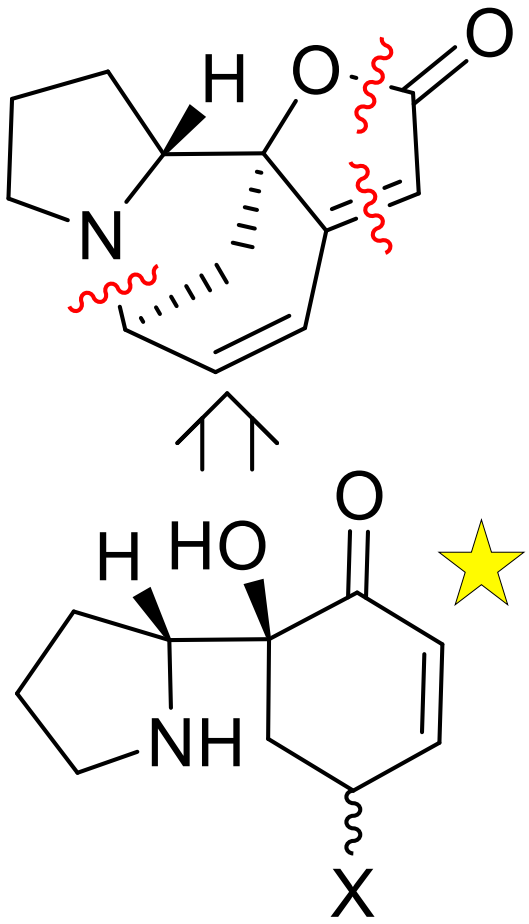
- *Fluegga virosa* of Euphorbiaceae

The Securinega Alkaloids

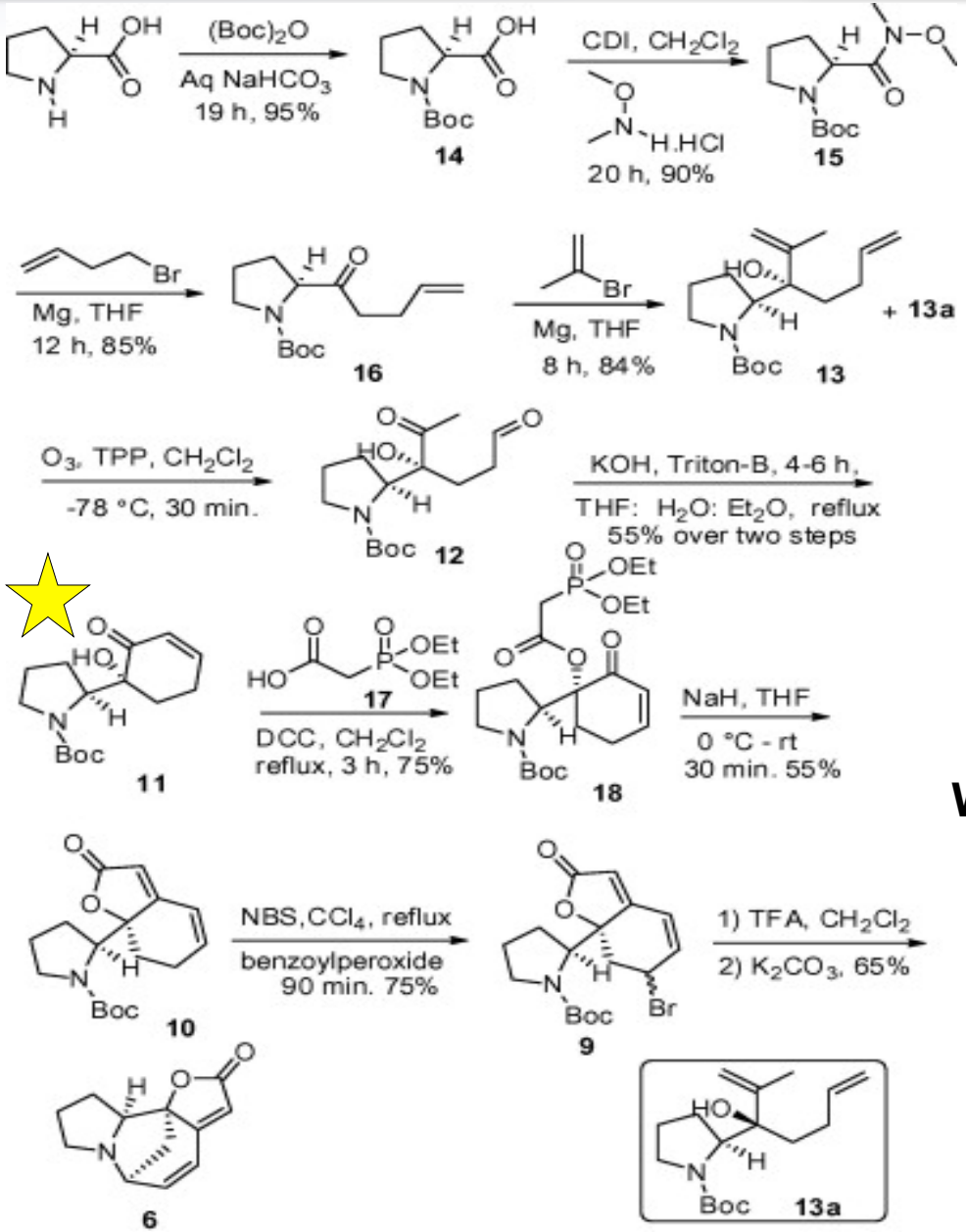


Norsecurinine Retrosynthetic Analysis

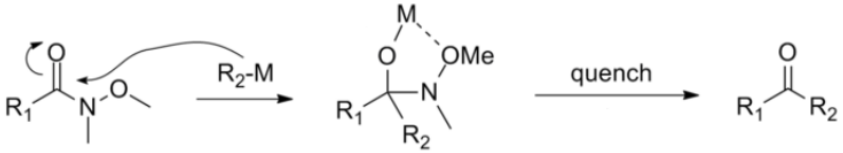




Allonorsecurinine (Reddy & Srihari, 2012)



Weinreb-Nahm Ketone Synthesis



Ozonolysis

Aldol Condensation

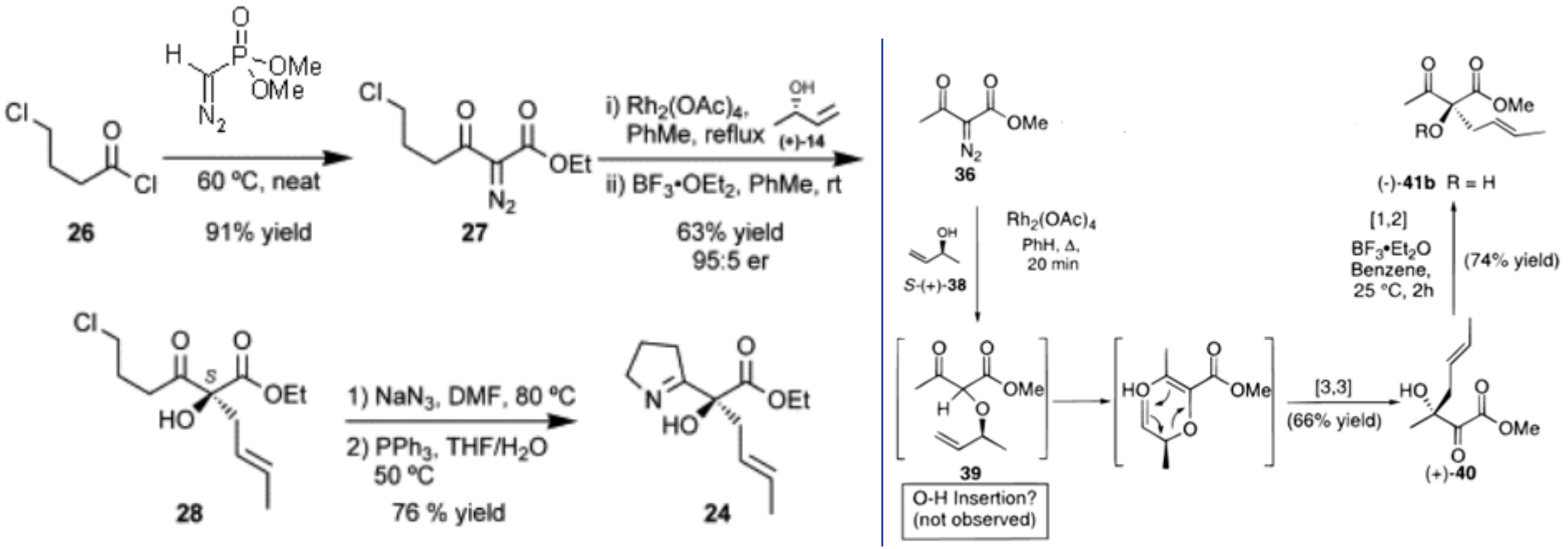
Wadsworth Emmons (Wittig Olefination)

Allylic Bromination

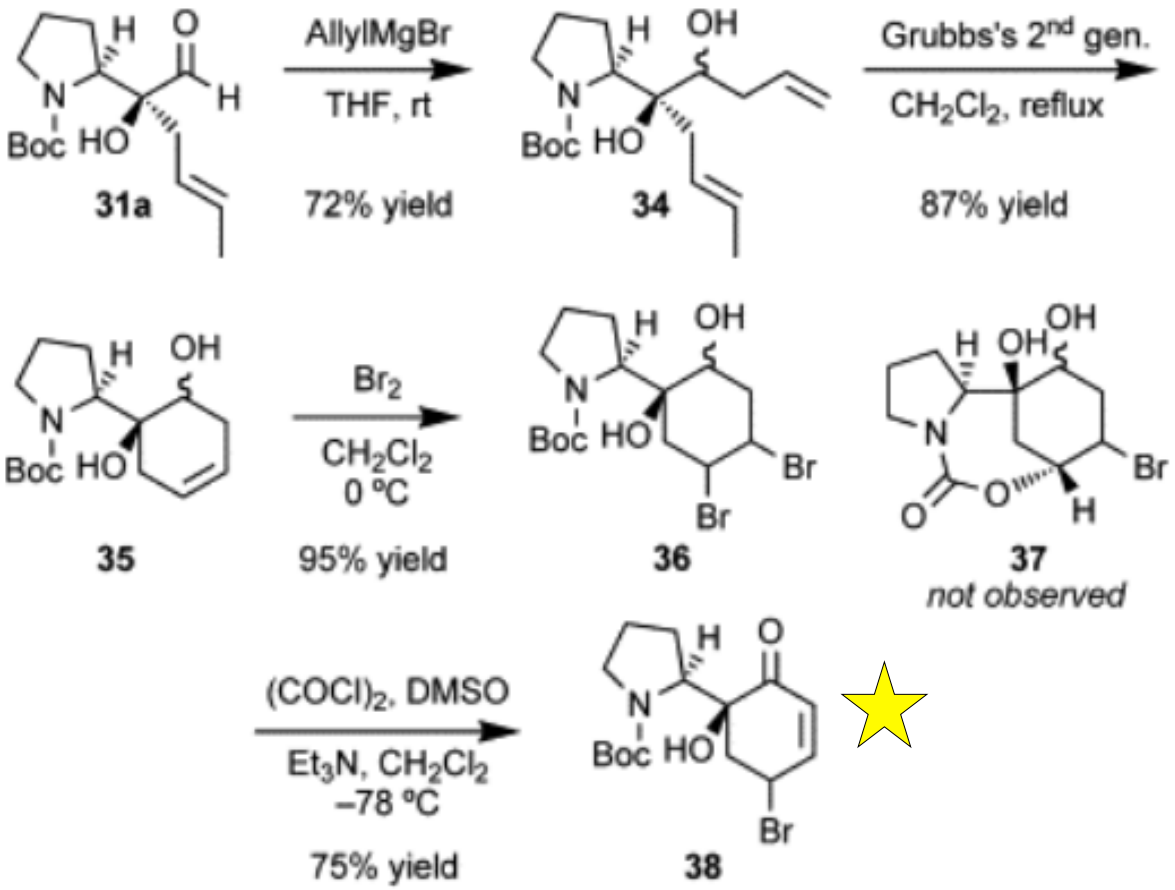
Boc Removal and N-Alkylation

Securinine (Medeiros & Wood, 2010)

Key Step: Rhodium Carbenoid-initiated O-H insertion / Claisen Rearrangement / 1,2-Allyl Migration domino process

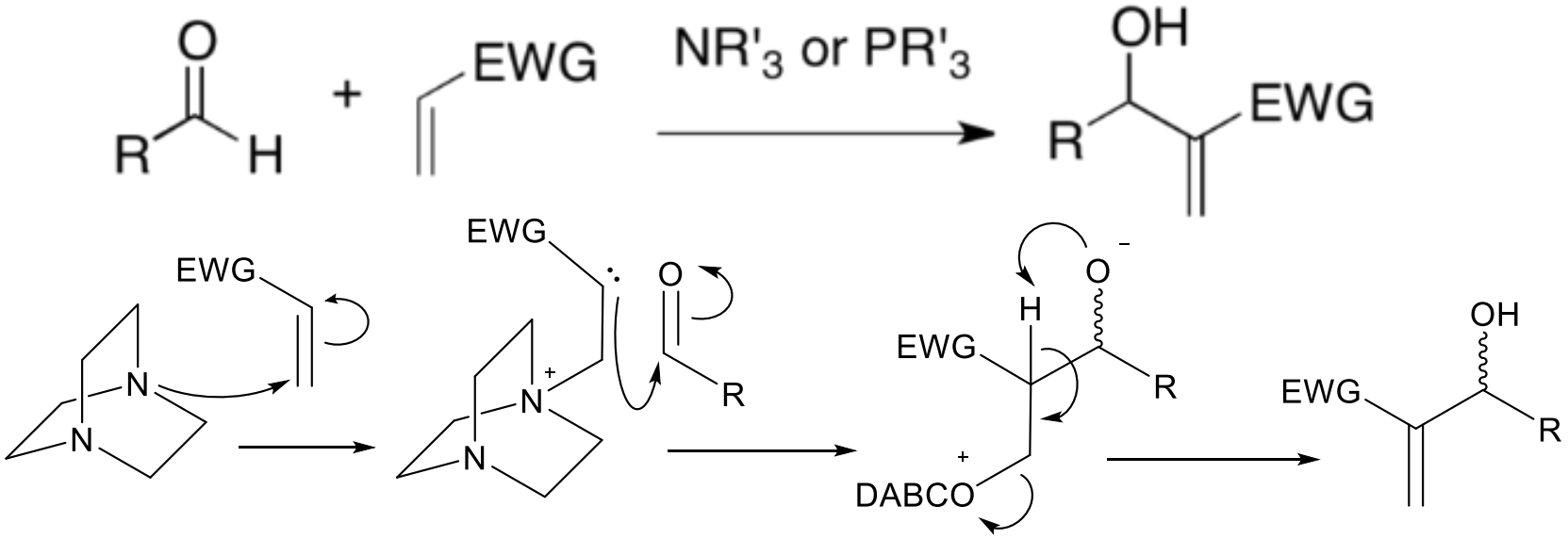


Norsecurinine (Medeiros & Wood, 2010)



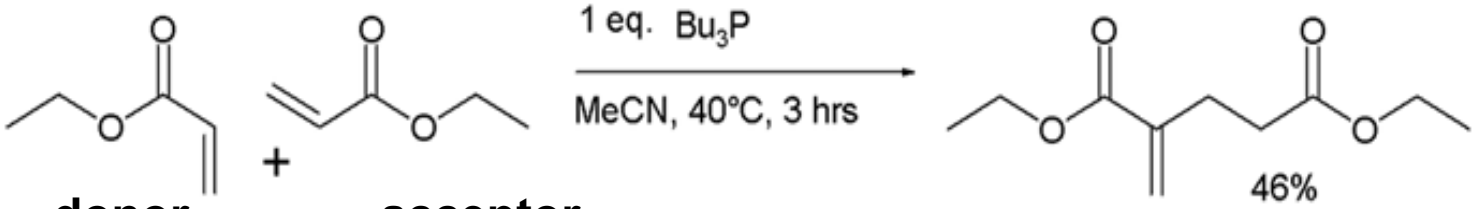
The Rauhut-Currier Reaction

- The Morita-Baylis Hilman Reaction

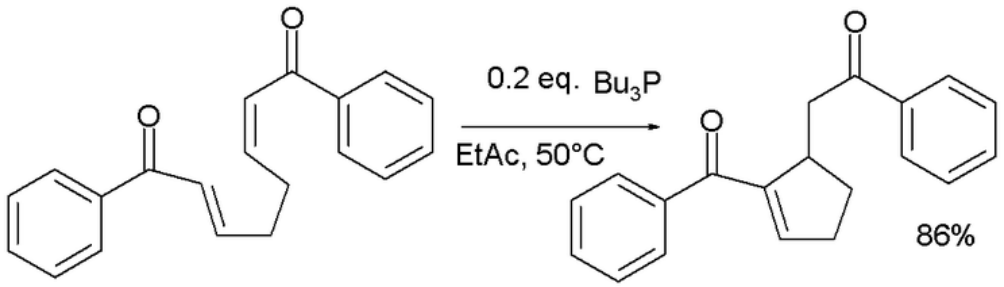


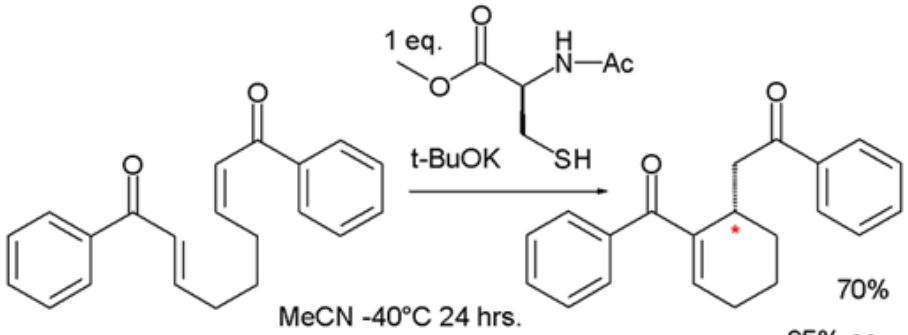
- Rauhut-Currier: The "Vinylogous Morita-Baylis Hilman Reaction"
  - Forms bond between **Alpha'** and **Beta"** positions of **ENONES**
  - Low Selectivity in hetero-couplings
  - Less Reactive / Kinetically Unfavored

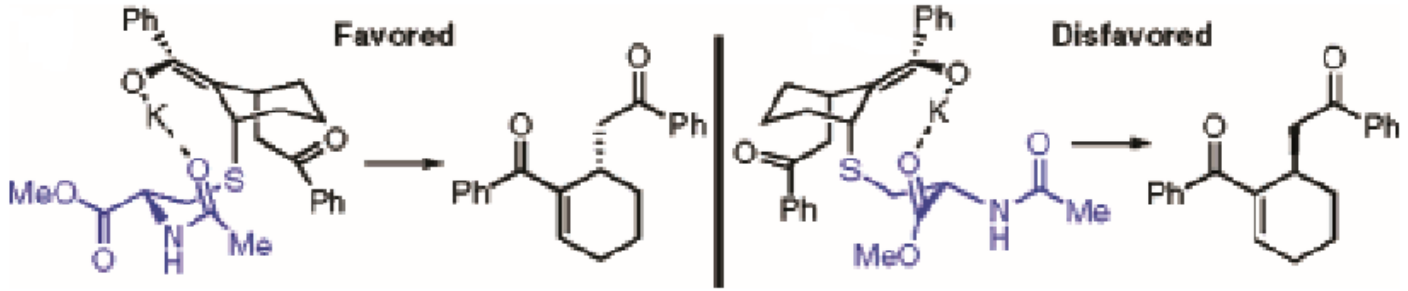
The Rauhut-Currier Reaction Precedence



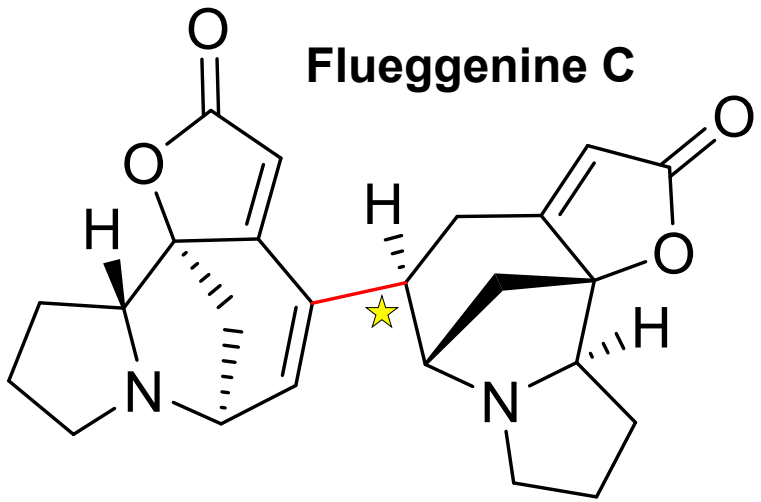
donor **acceptor**

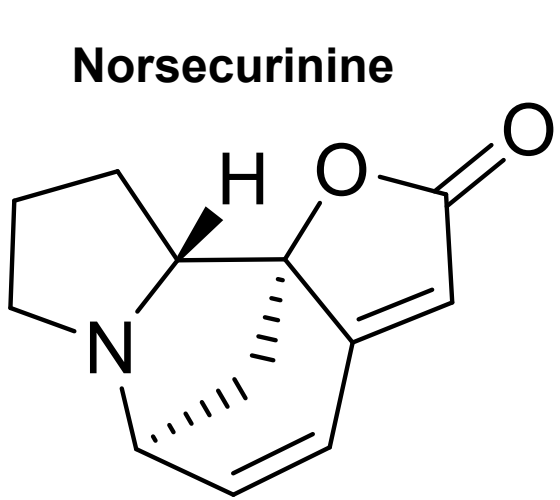


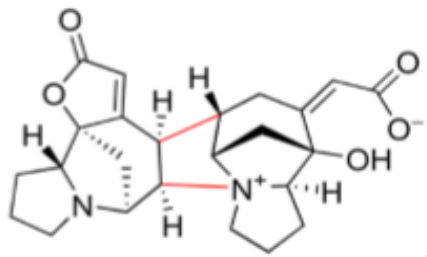




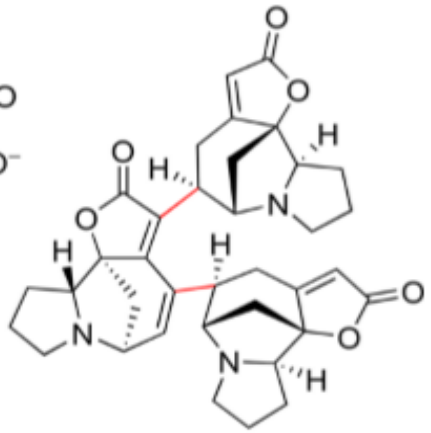
“Envisioned” Biosynthesis is Enzymatic RC



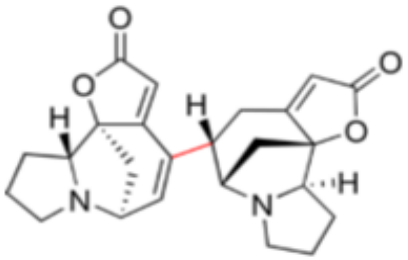




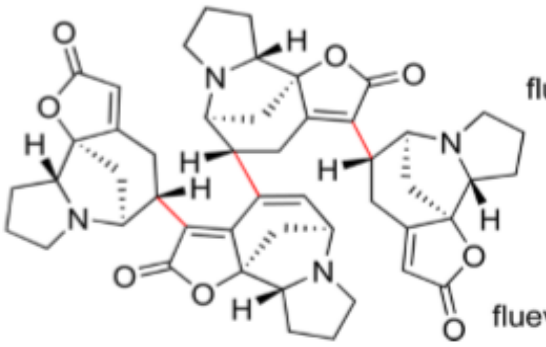
flueggenine B (**5**)



fluevirosine D (**7**)

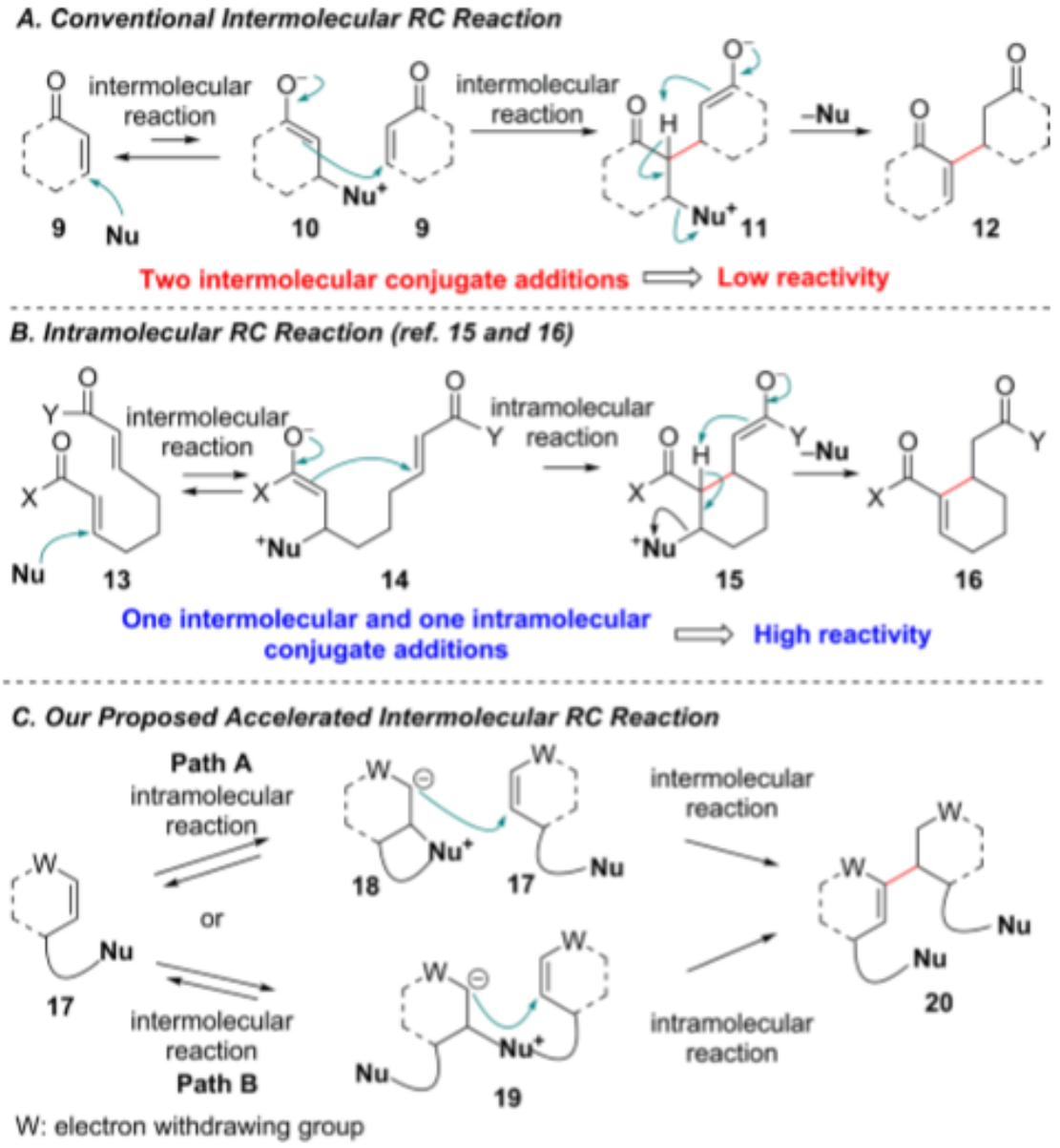


flueggenine A (**4**)

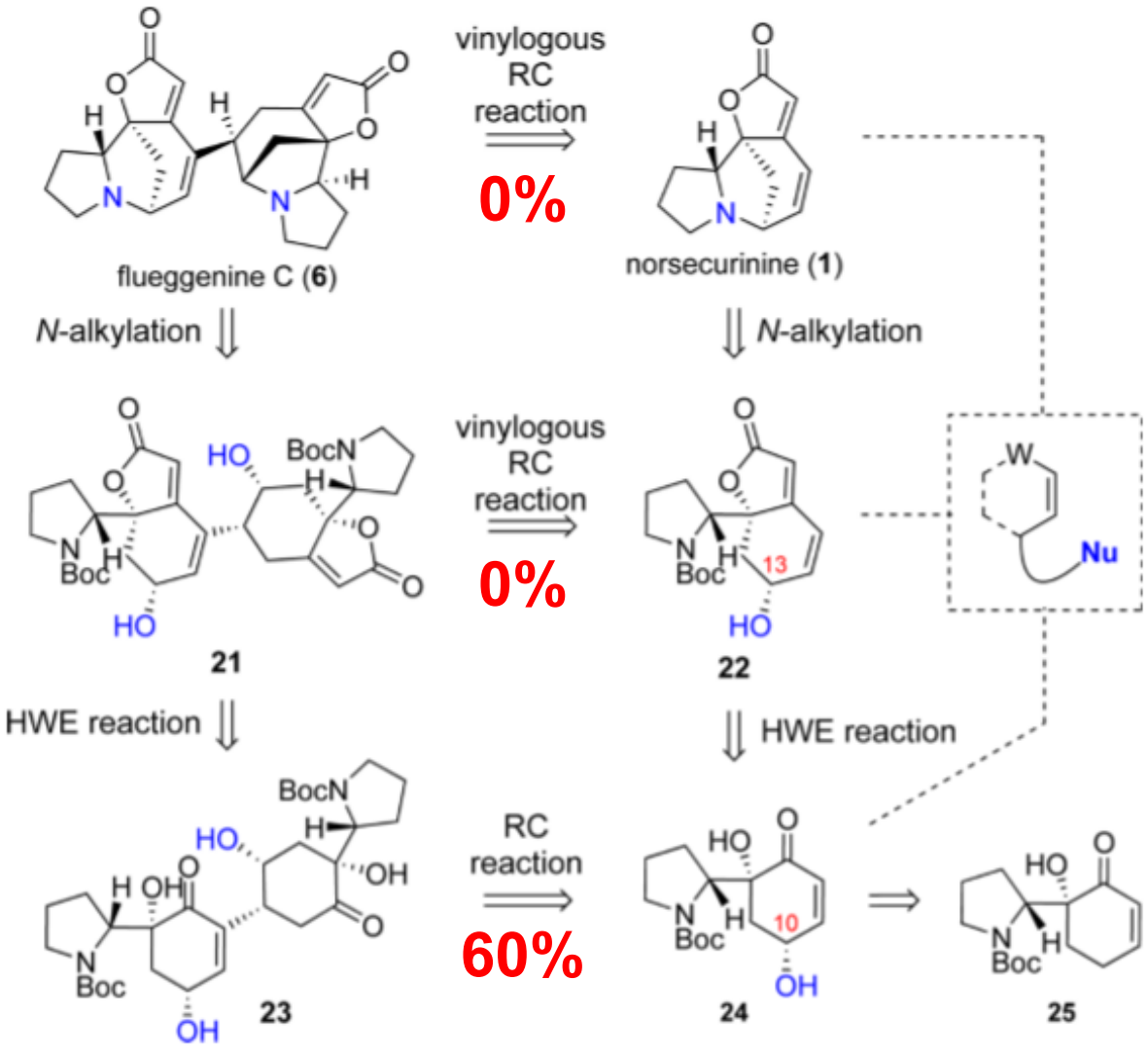


fluevirosinine A (**8**)

Overcoming Limitations of the Conventional RC

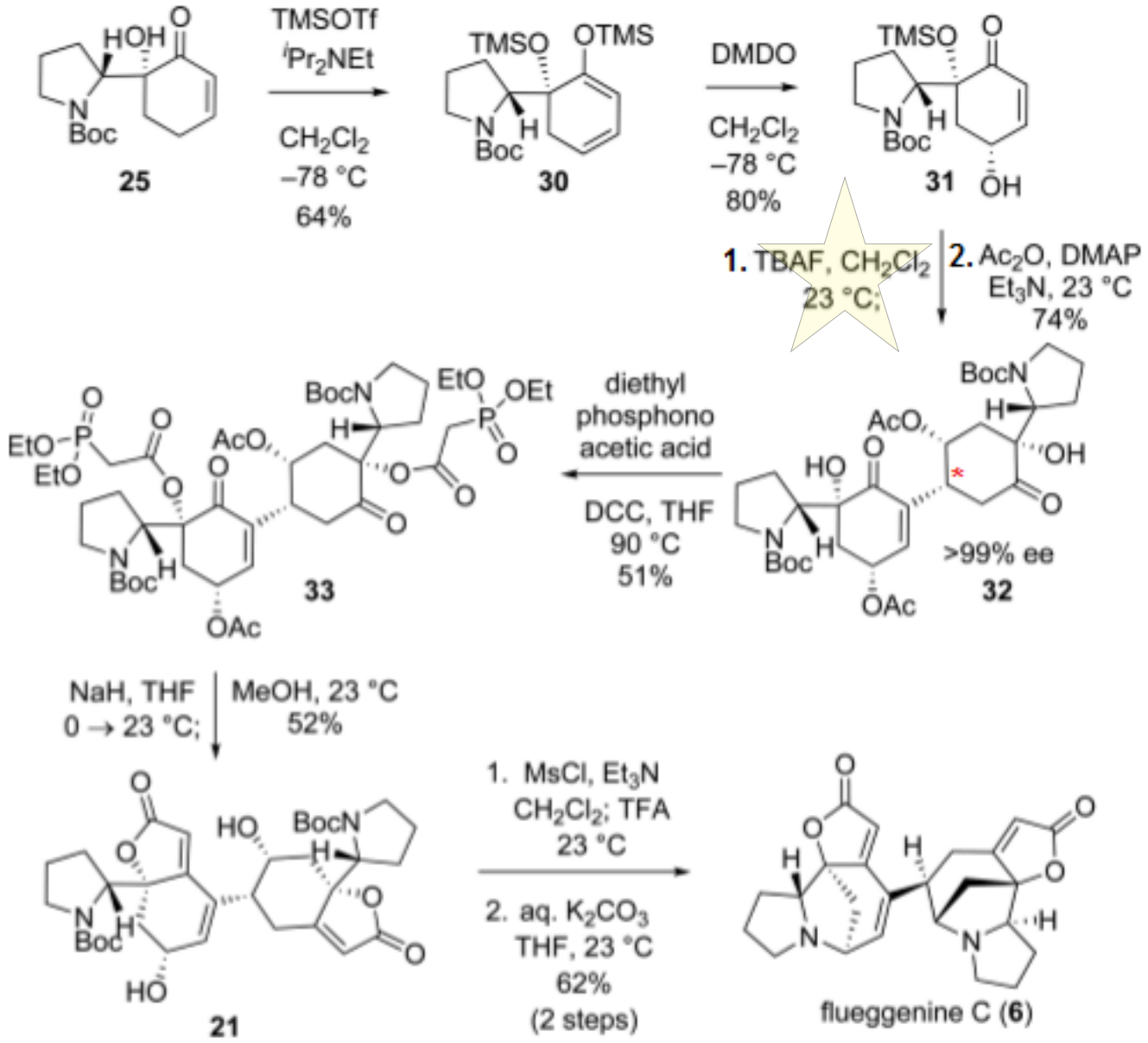


Bringing it All Together

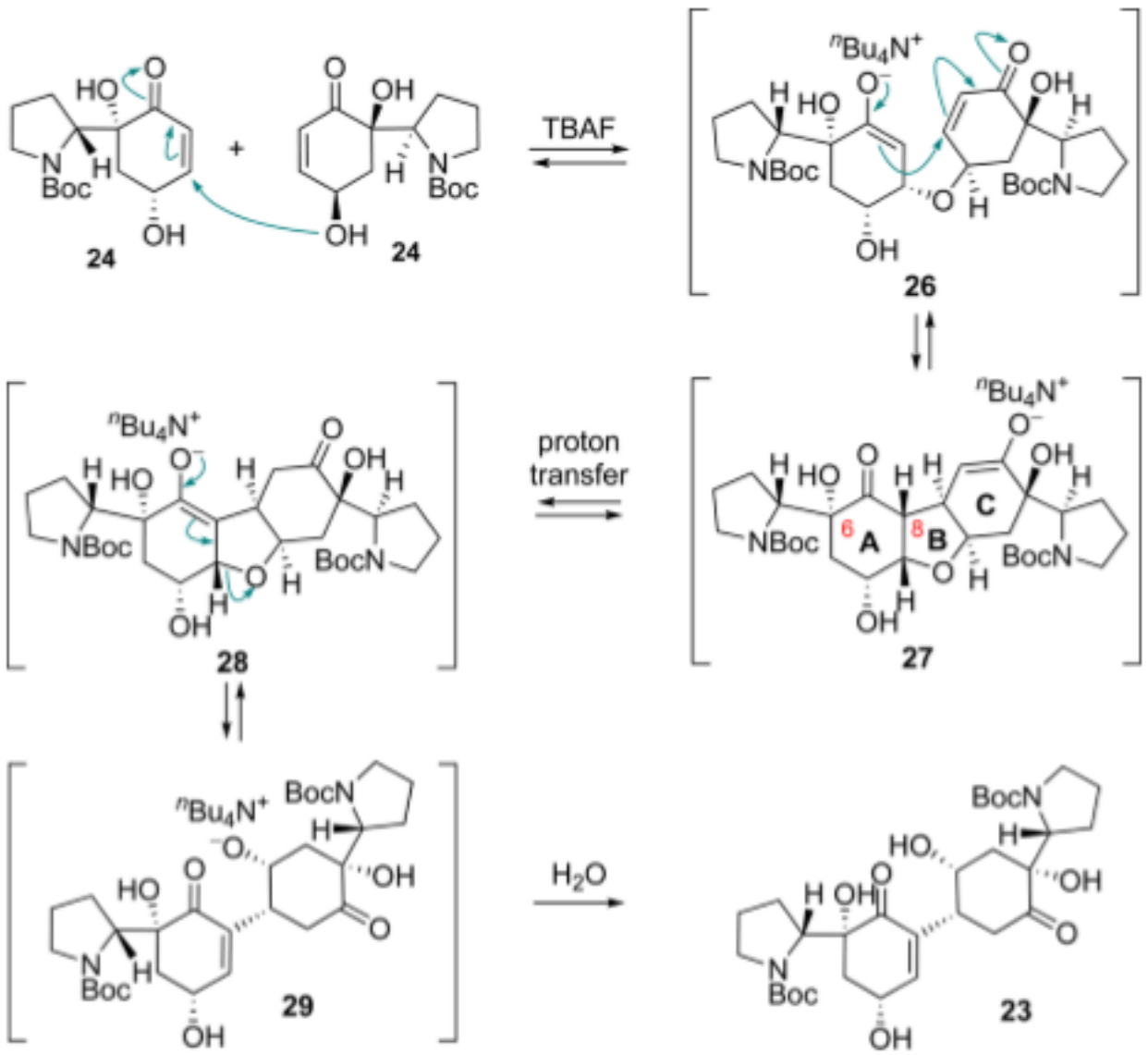


Blue – Tethered Base

Total Synthesis



Proposed Mechanism



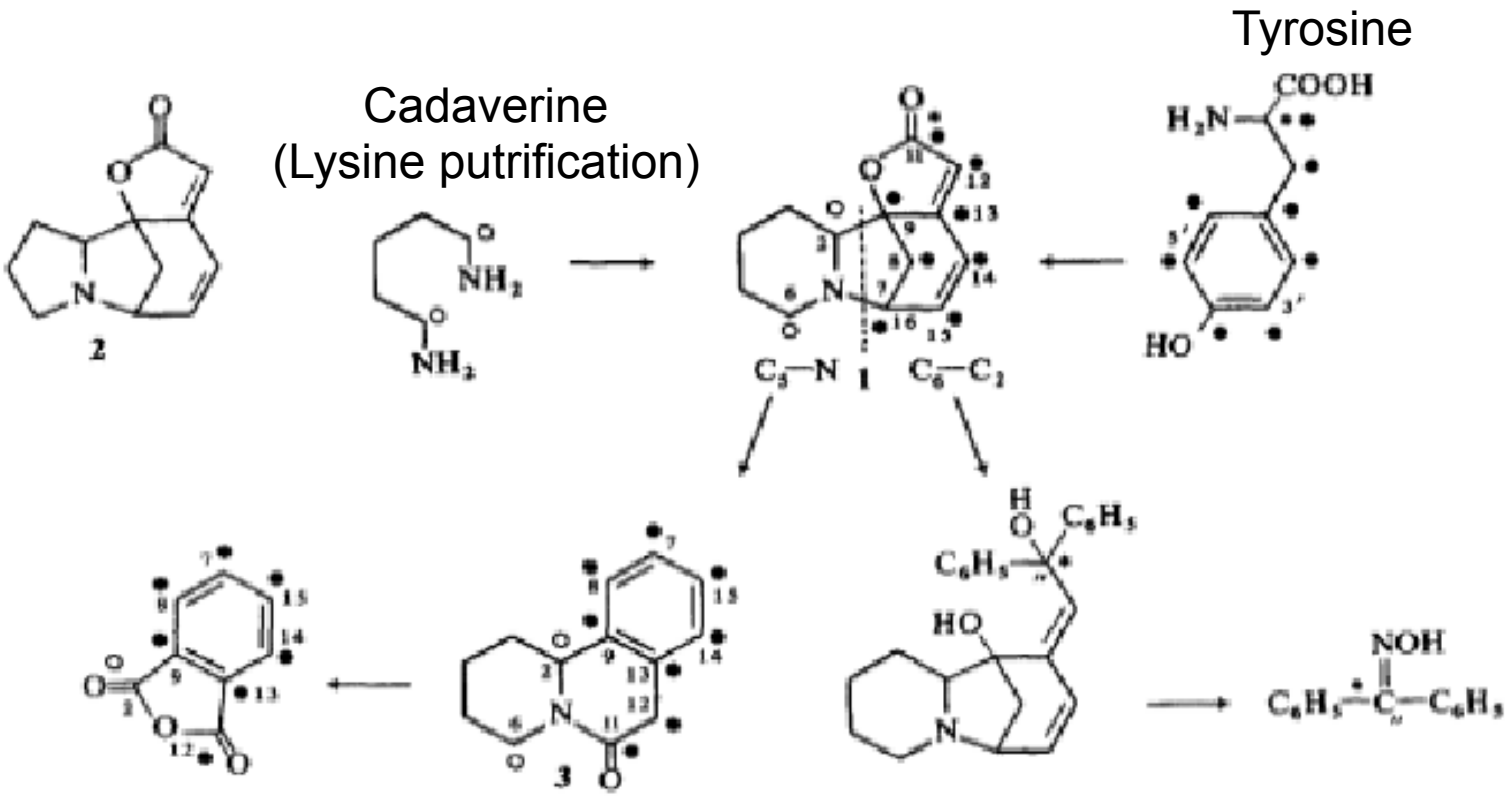
Criticisms and Conclusions

- Limited Reagent Conditions Tested
  - Reagent Identity (3)
  - EQ Reagent
  - Reaction Time (inconsistent)
  - Reagent Concentrations
  - Solvent System
  - Temperature
  - Enone Substrate (3)
- Flueggenine C vs. Flueggenine A - “Wrong Product”
- Support for the Mechanism is Weak

- Achieved the total synthesis of Flueggenine C in 12 Steps from Boc-D-Proline in overall 1.7% yield
- First use of intramolecular Rauhut Currier Reaction for the formation of Securinine Alkaloids

Questions?

Securinine Biosynthesis



http://www.sciencedirect.com/science/article/pii/0031942277800150

References

- http://www.westafricanplants.senckenberg.de/images/pictures/flueggea_virosa_ms_1792_748_e35d43.jpg (picture)
- http://pubs.acs.org/doi/pdf/10.1021/ja067139f
- http://www.sciencedirect.com/science/article/pii/S004040201000369 8
- http://pubs.acs.org/doi/pdf/10.1021/ja9713035
- http://pubs.acs.org/doi/pdf/10.1021/jacs.7b02751 (featured)
- http://ac.els-cdn.com/0031942277800150/1-s2.0-0031942277800150-main.pdf?_tid=c7146b40-5774-11e7-be27-00000aab0f02&acdnat=1498154652_35608af31c5af522da334bfcc7deccc0 (bio)
- http://www.sciencedirect.com/science/article/pii/S004040201000369 8