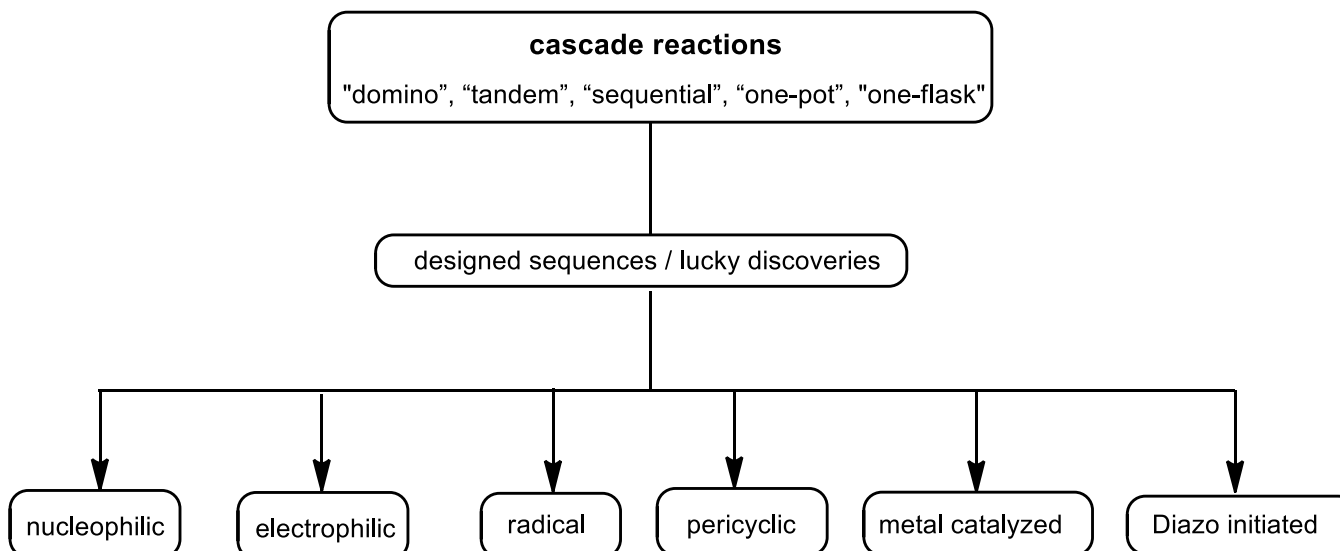

Cascade Reactions

Magnus Pfaffenbach
Gaich-Group Seminar
November 12, 2012

Overview and Definition

Definition (strict):

A cascade reaction is a process in which several bonds are formed in sequence without isolating intermediates, changing conditions or adding reagents.



Pro and Contra

Practical Advantages:

- Atom economy
- Reduction of time, labor, waste and resources
- „Green Chemistry“

Academic Considerations:

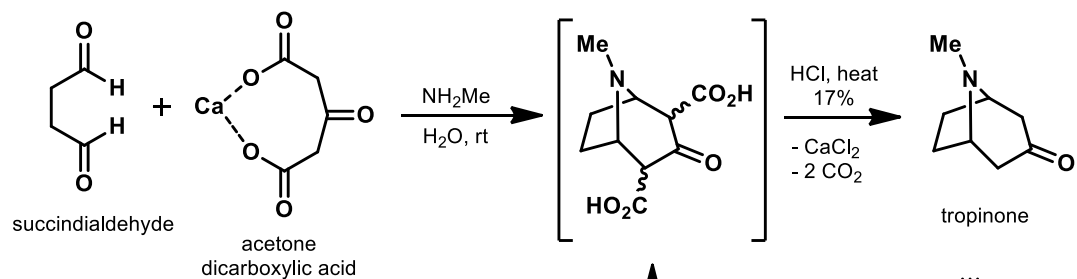
- Fast access to structures with increased complexity
- Aesthetic appeal to synthetic planning

Disadvantages:

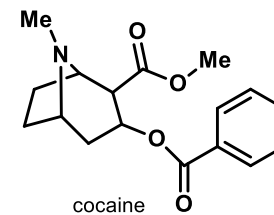
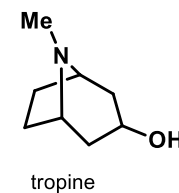
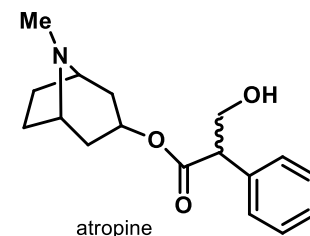
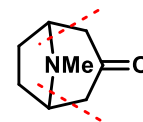
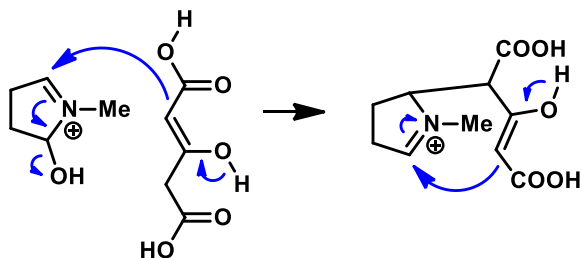
- Synthesis of precursors often far from trivial
- Few examples of catalytic enantioselective cascade reactions

Classic Examples

Robinson's one-flask total synthesis of tropinone

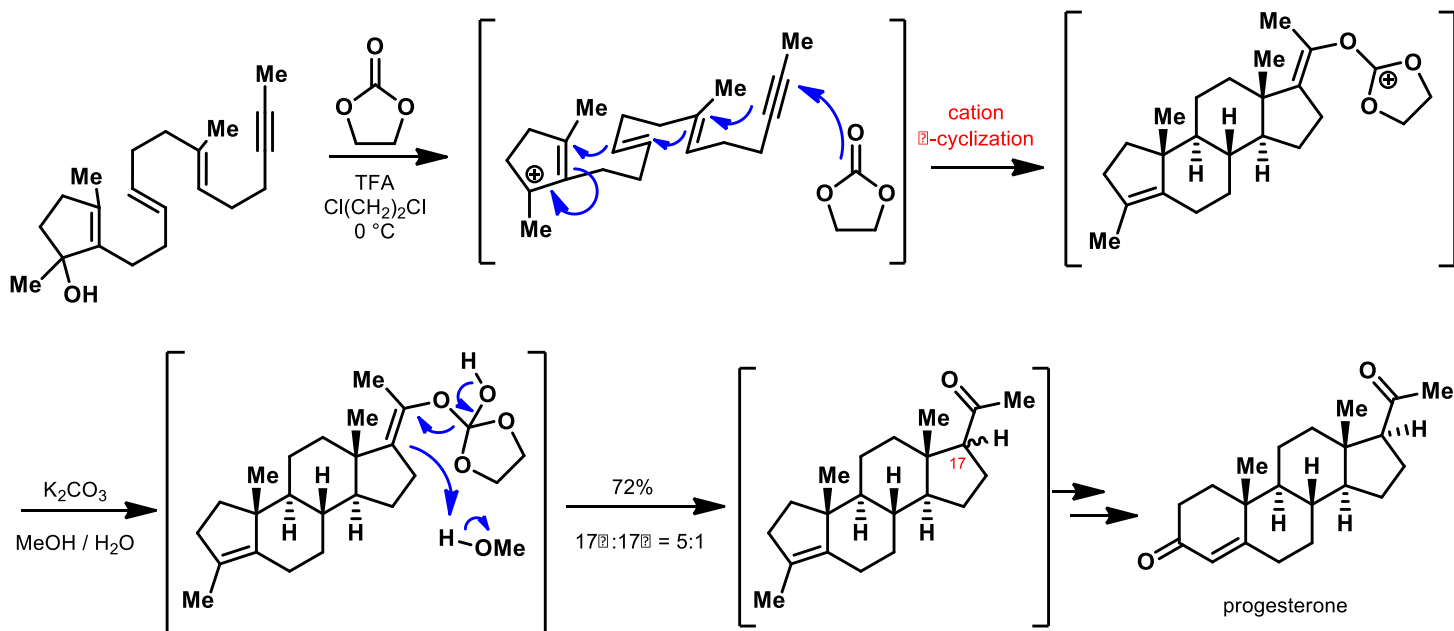


Mechanism:



Classic Examples

The total synthesis of progesterone involving a polyolefin cyclization



Johnson et al.,

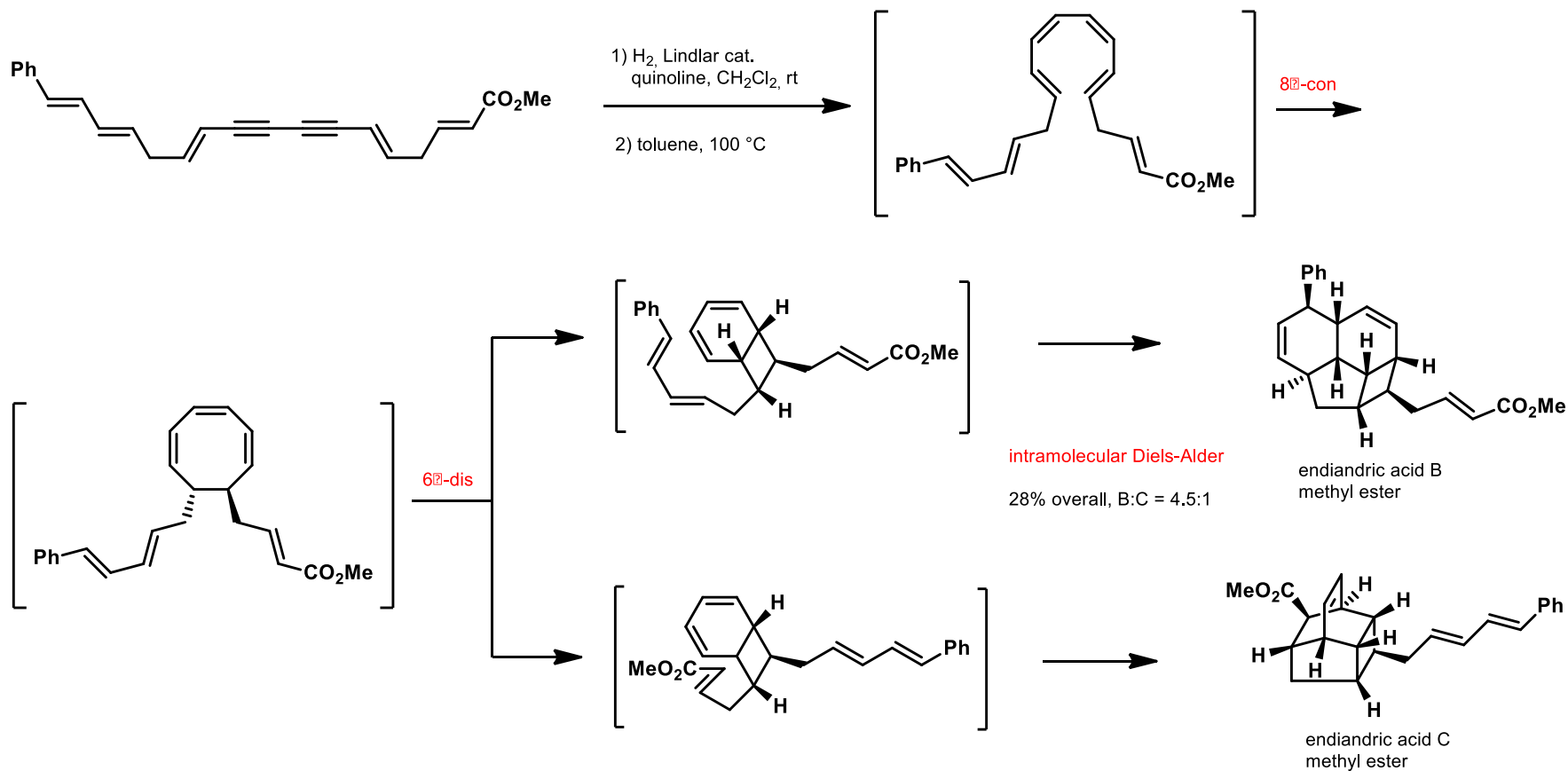
a) *J. Am. Chem. Soc.* **1971**, *93*, 4332-4334;

b) *J. Am. Chem. Soc.* **1978**, *100*, 4274-4282.

(on the basis of the Stork-Eschenmoser hypothesis)

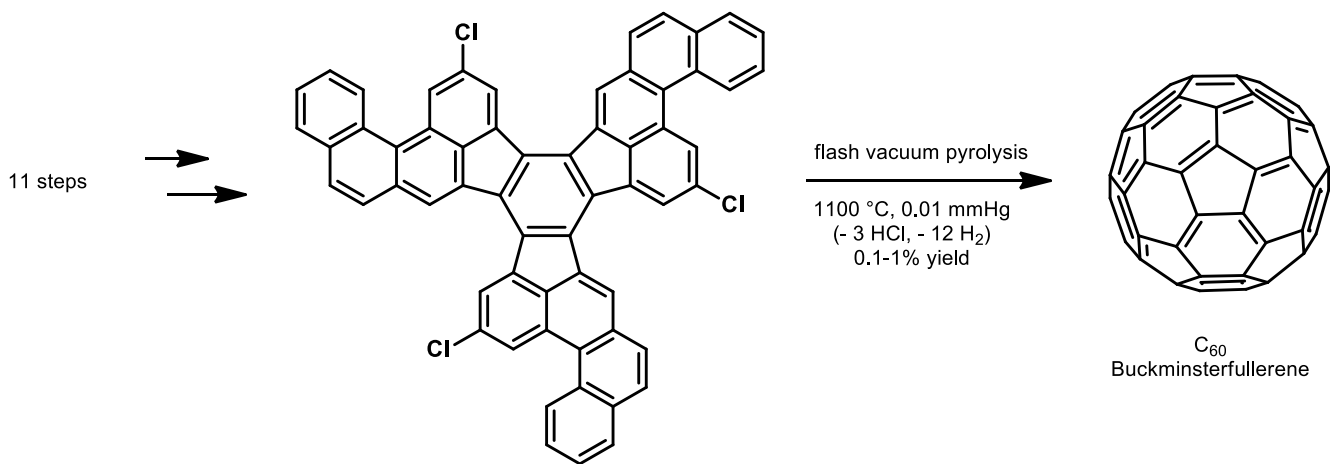
Classic Examples

The endiandric acid cascade



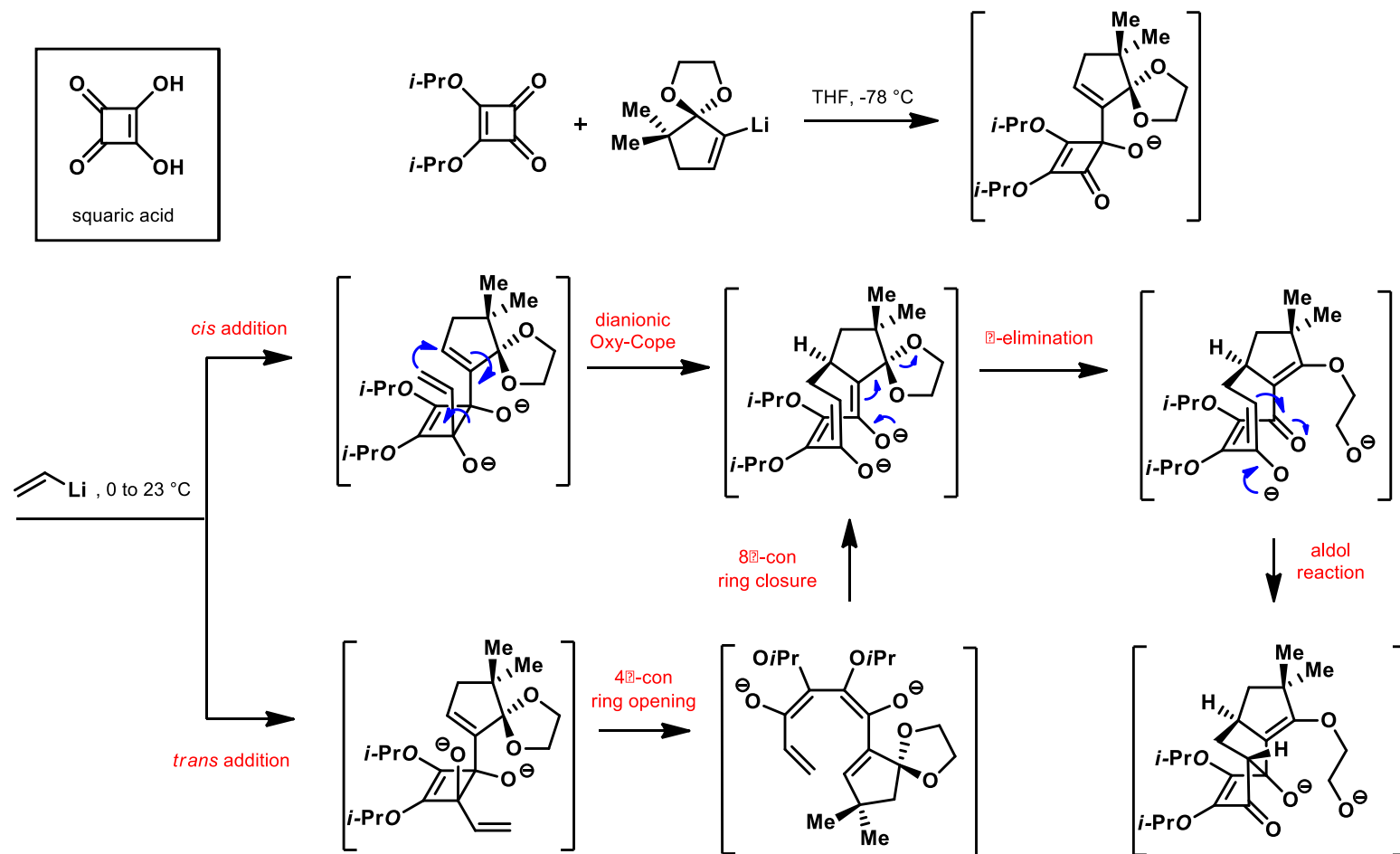
Classic Examples

The total synthesis of C_{60}

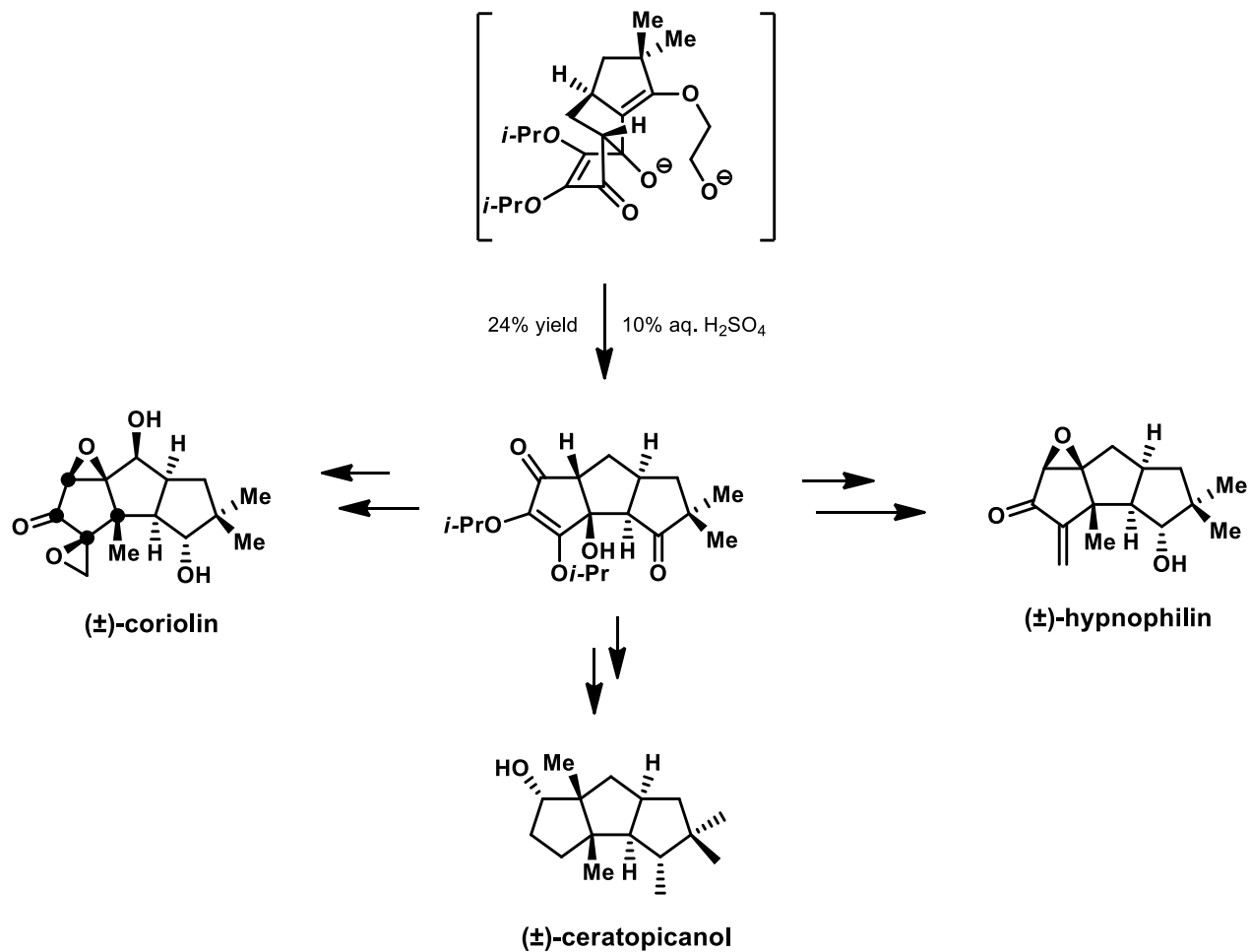


Nucleophilic Cascades

The squarate ester cascade in the total synthesis of (±)-hypnophilin and (±)-coriolin

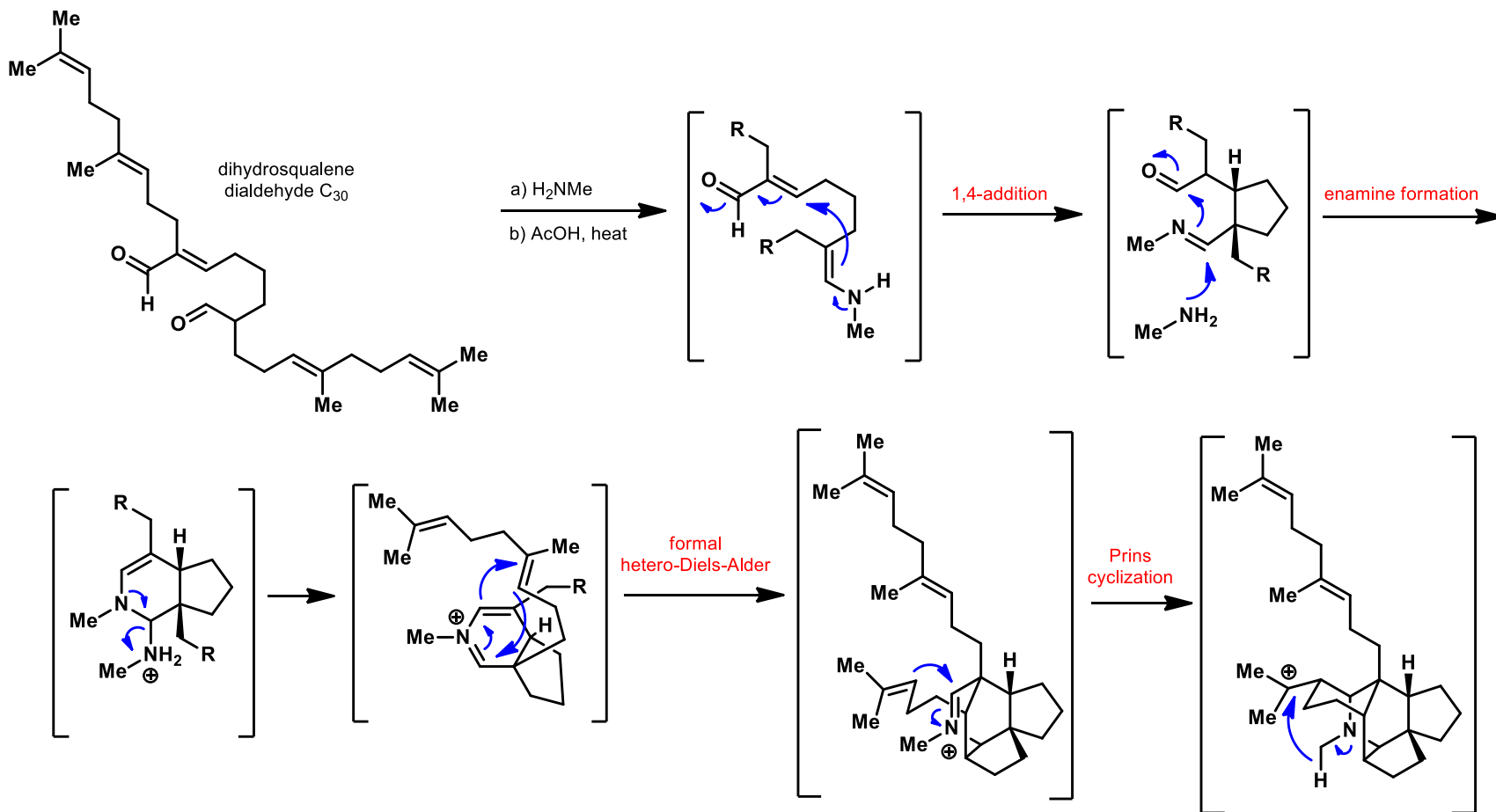


Nucleophilic Cascades

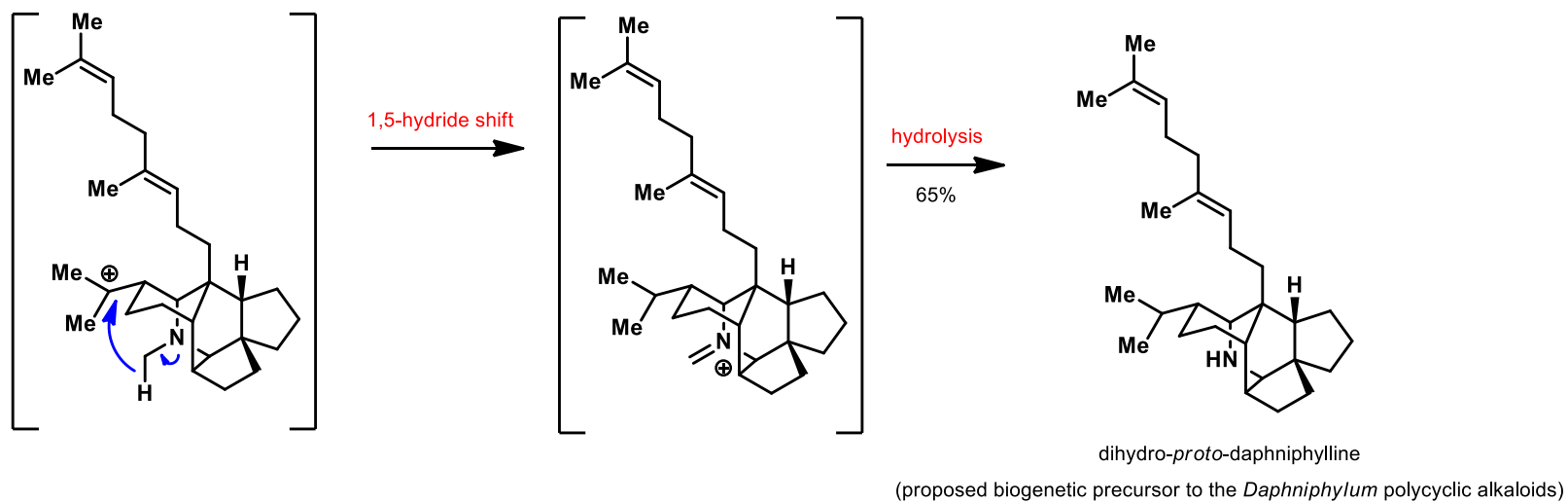


Electrophilic Cascades

Biomimetic synthesis of dihydro-*proto*-daphniphylline

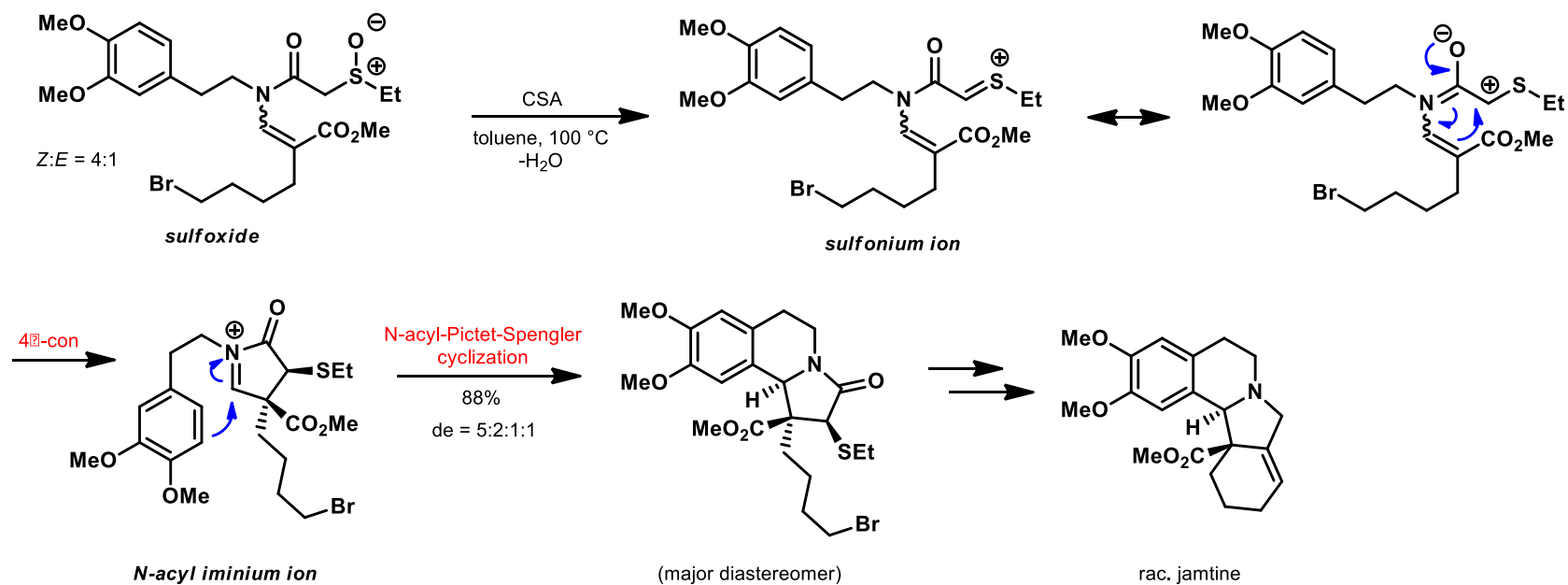


Electrophilic Cascades



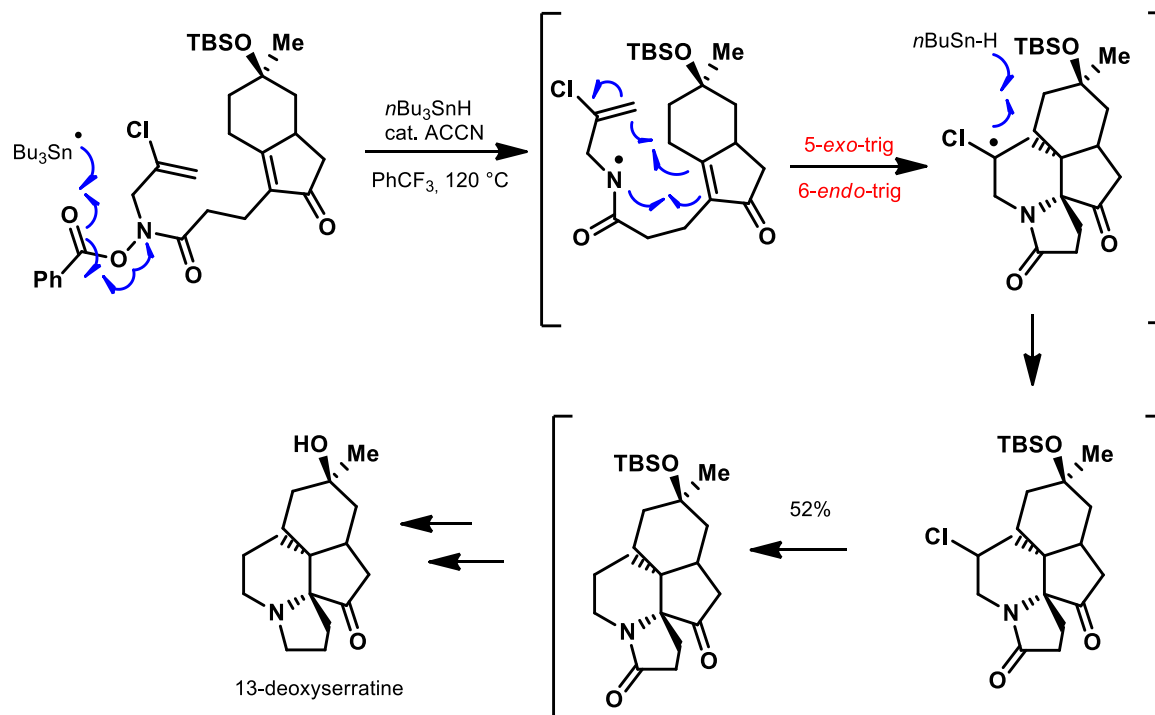
Electrophilic Cascades

Total synthesis of jamine through a Pummerer / Pictet-Spengler cascade



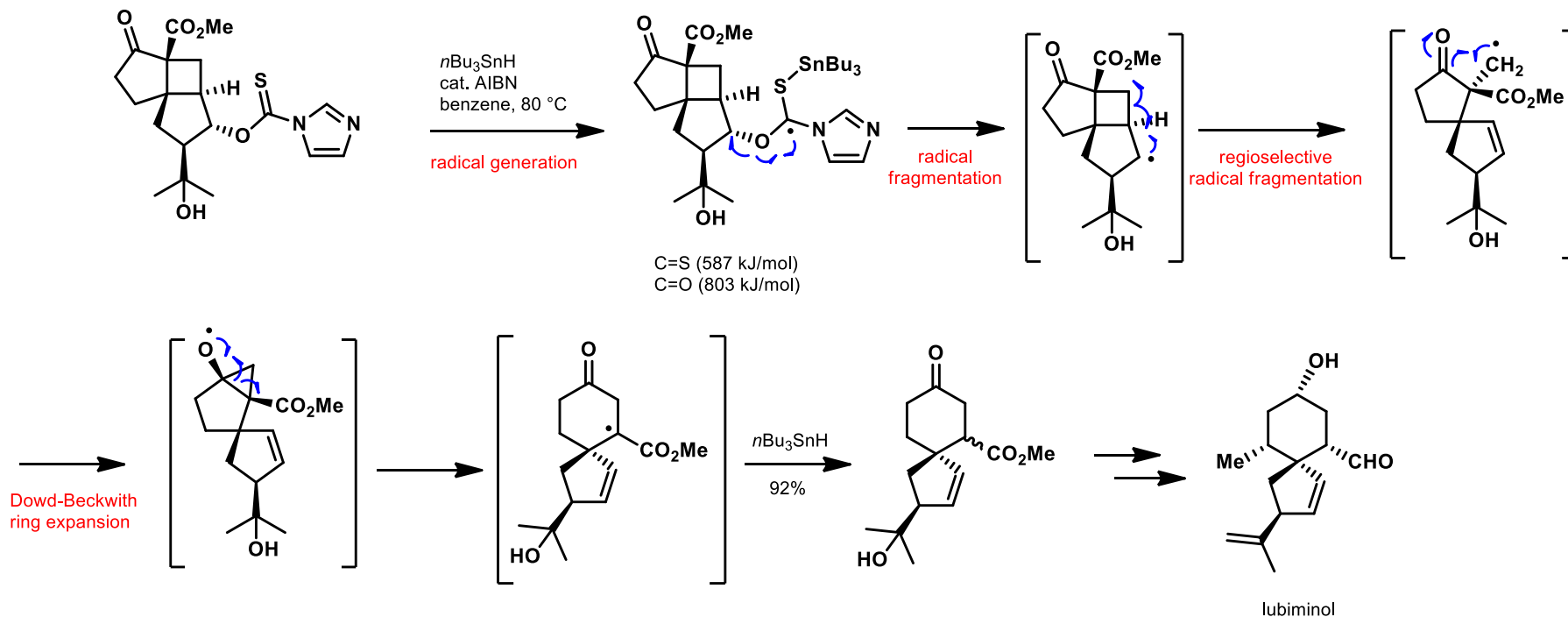
Radical Cascades

Nitrogen-centered radical cyclization in the total synthesis of 13-deoxyserratine



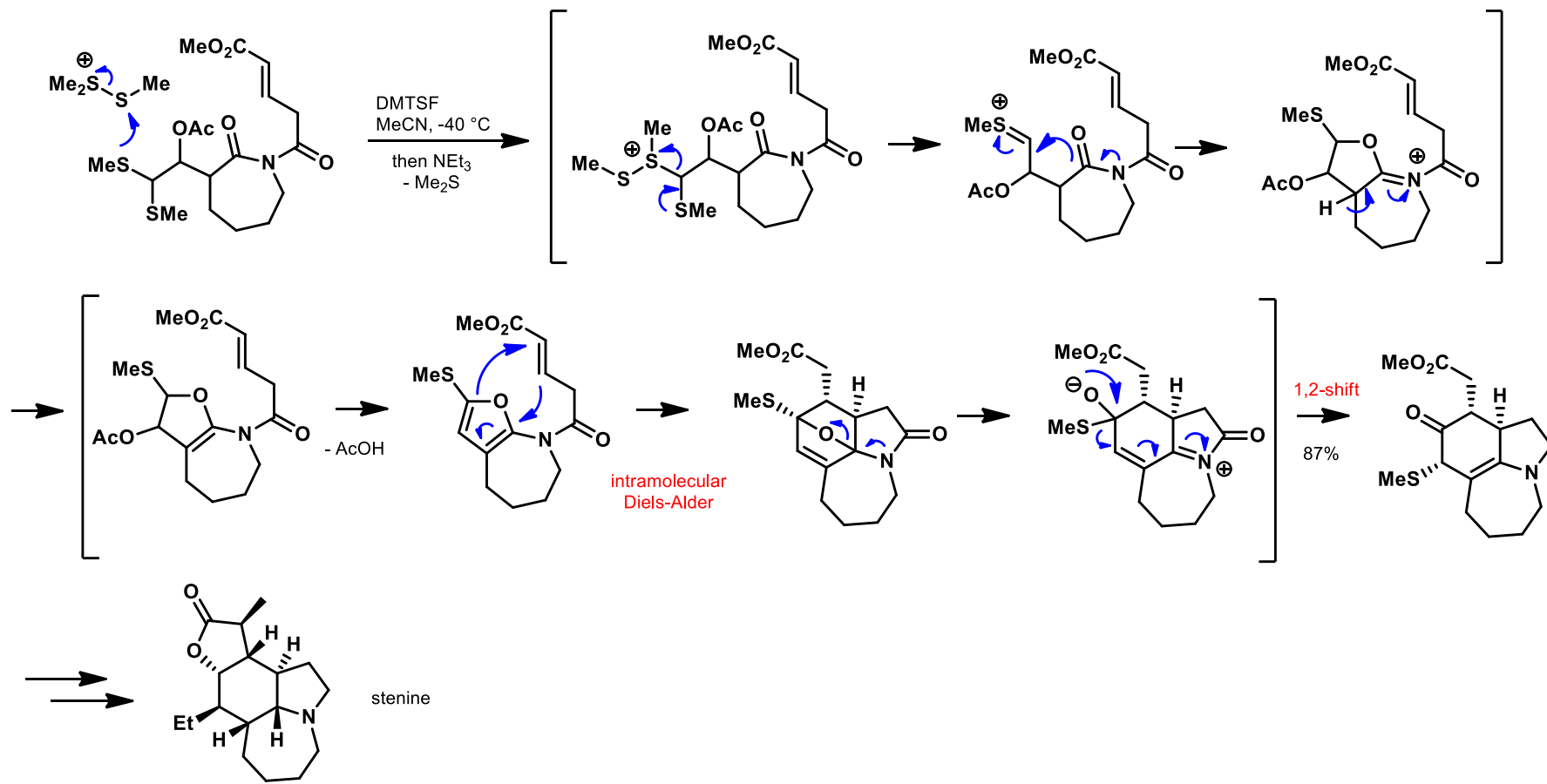
Radical Cascades

Total synthesis of lubiminol through a cyclobutane fragmentation / ring expansion cascade



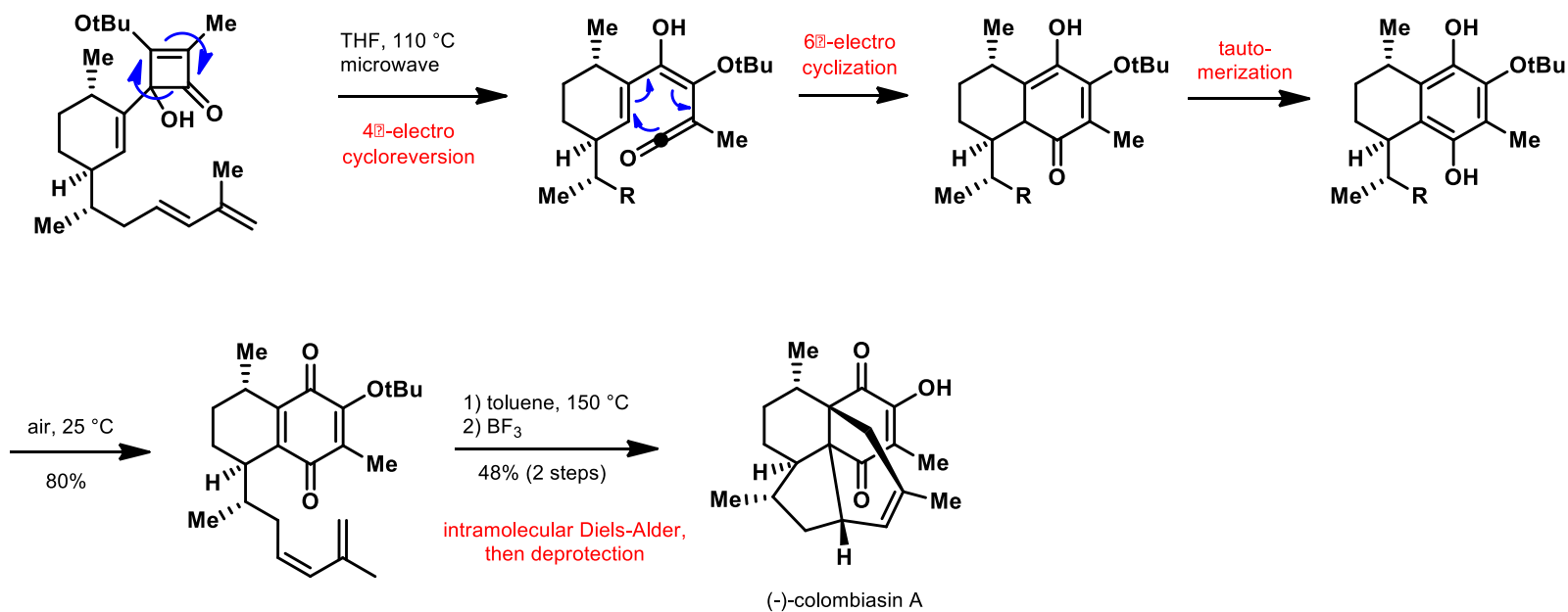
Pericyclic Cascades

A heterocyclization/Diels-Alder reaction/rearrangement cascade in the total synthesis of stenine



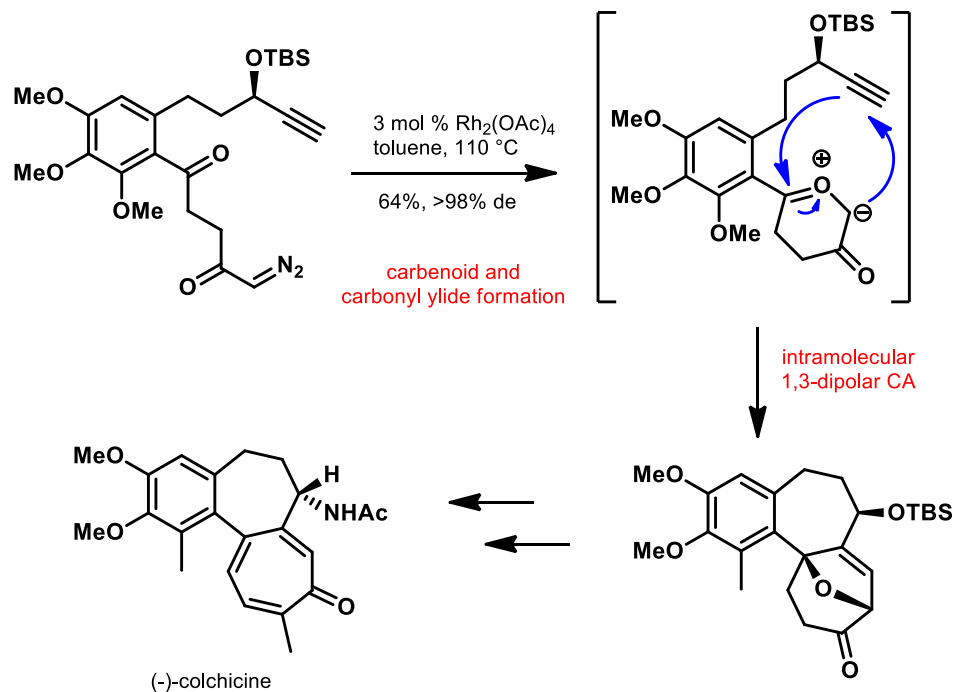
Pericyclic Cascades

Electrocyclization reactions in the synthesis of (-)-colombiasin A



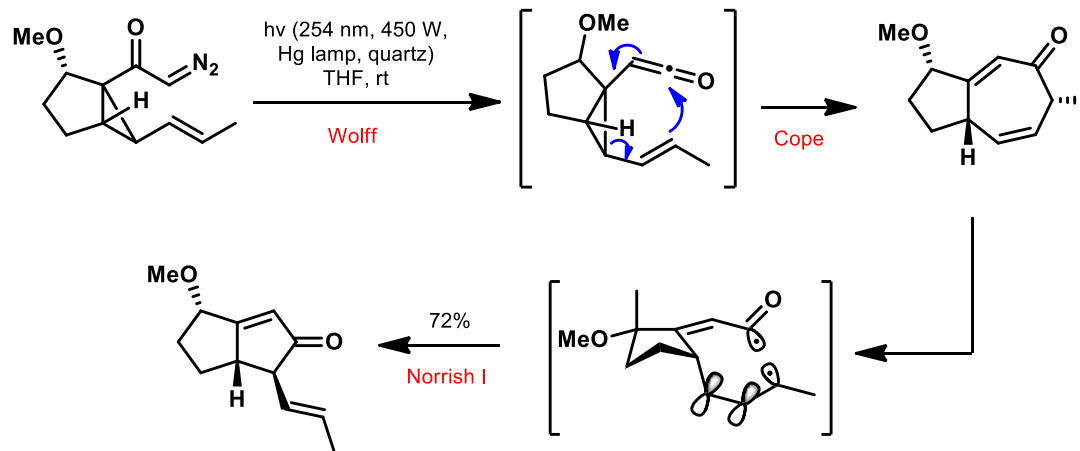
Transition Metal-Catalyzed Cascades

A tandem carbonyl ylide formation/1,3-dipolar CA approach to the synthesis of (-)-colchicine



Diazo Compound Initiated Cascades

Domino Wolff / Cope rearrangement / Norrish type I fragmentation / recombination process



Thank you for your attention!

Questions?