

The Enantioselective Dakin-West Reaction...

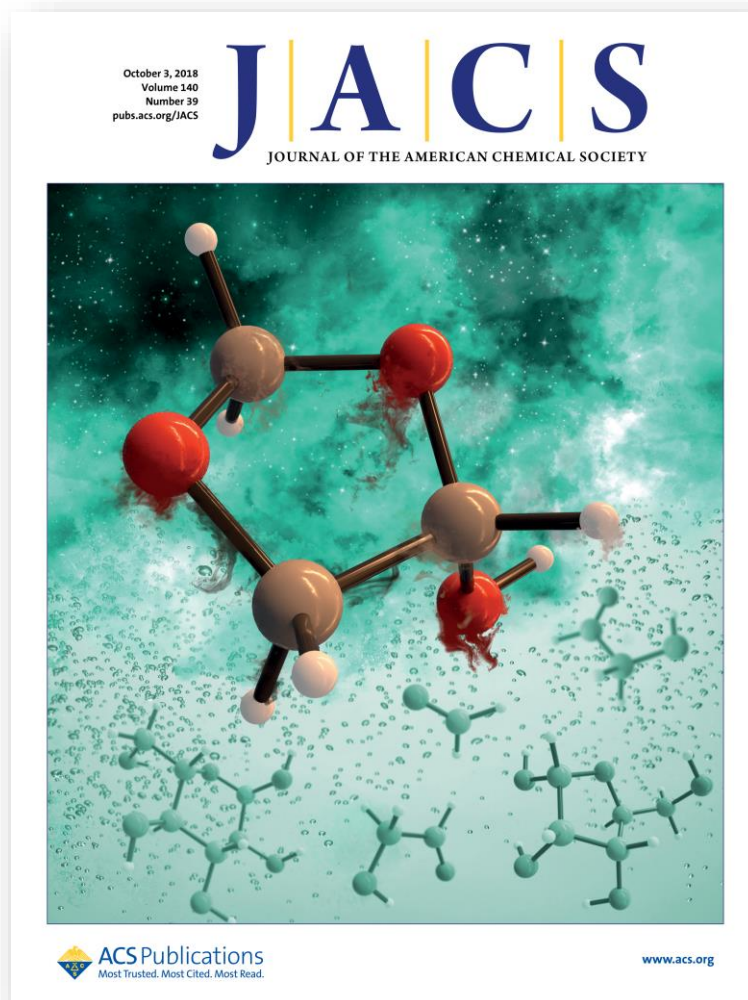
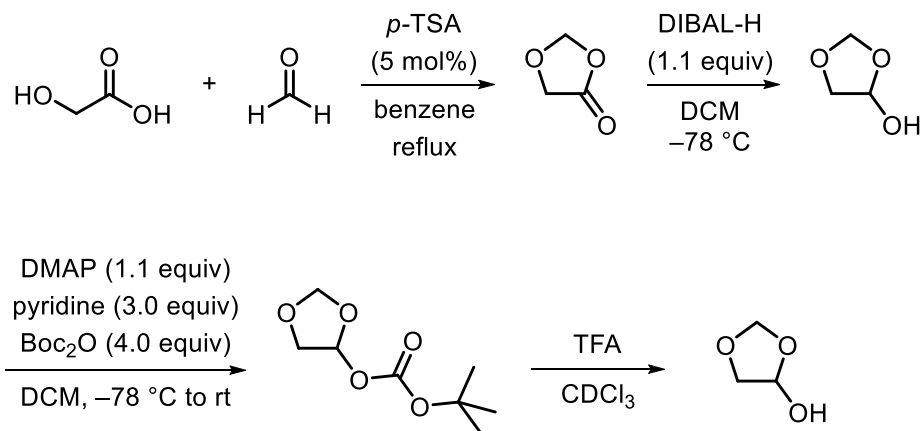
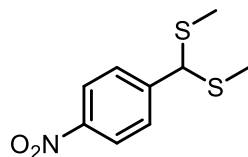
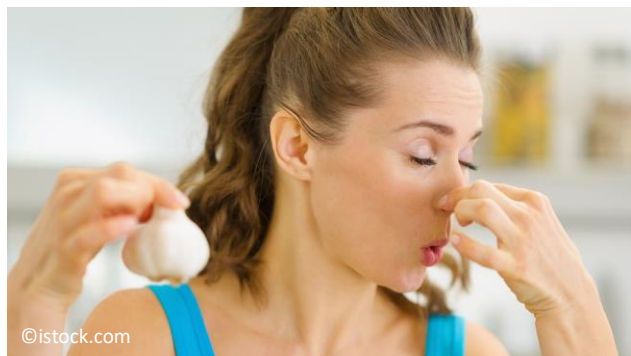
... and other things that preoccupied myself

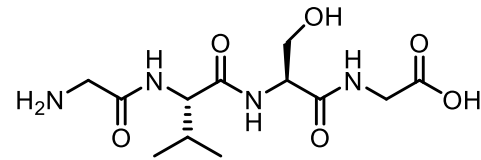
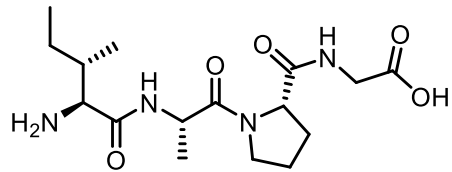
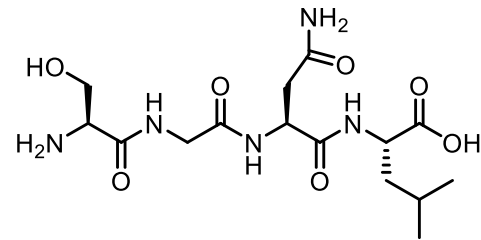
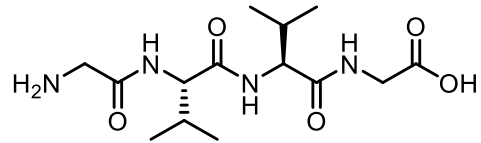
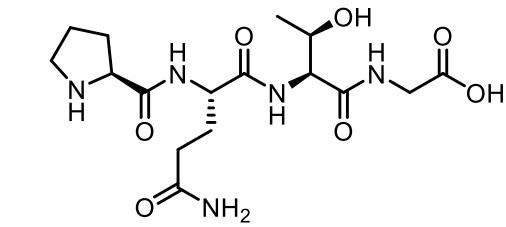
Group Seminar

01.03.2019

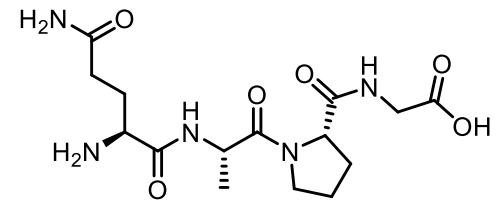
Raffael C. Wende

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Potential Testosteron Blockers

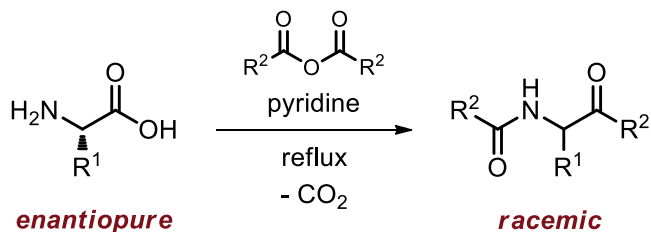


The Dakin-West Reaction

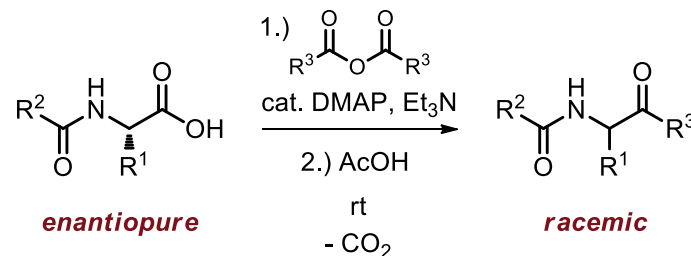


Simplicity...

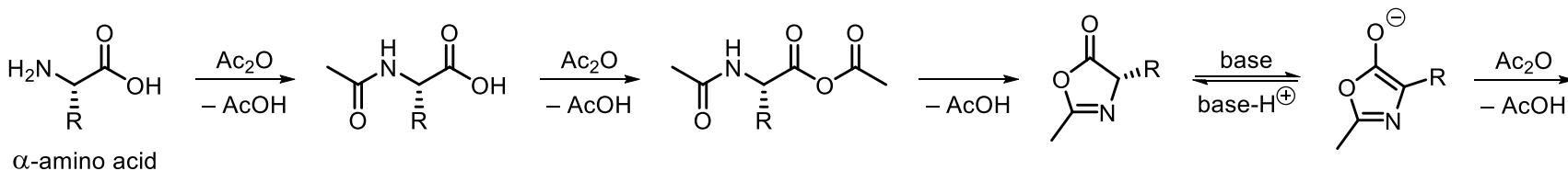
Dakin & West (1928):



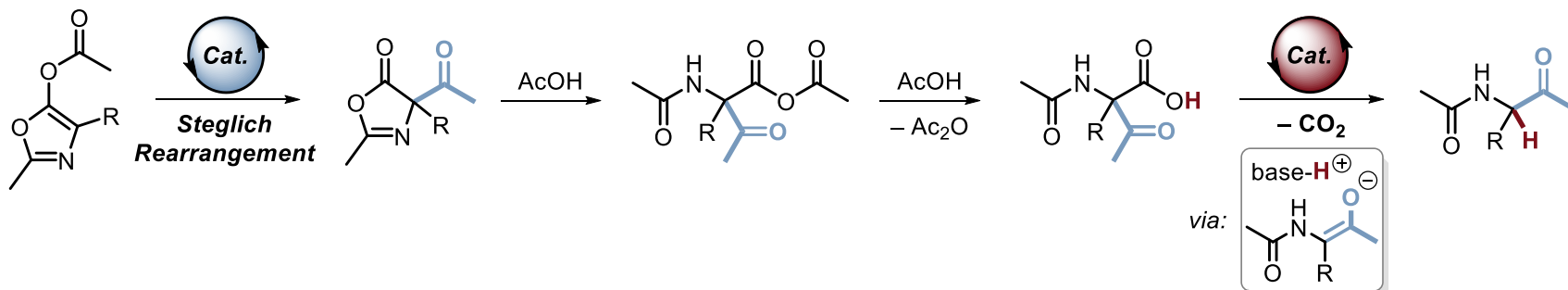
Steglich & Höfle (1969):



Complexity...

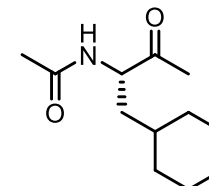
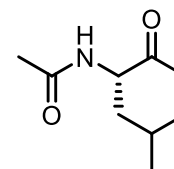
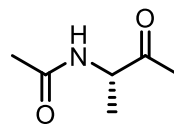
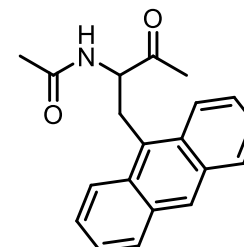
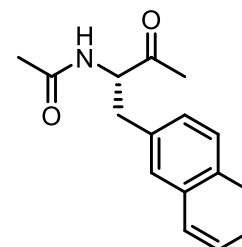
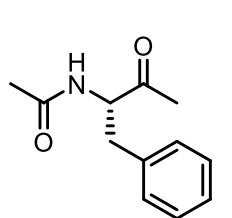
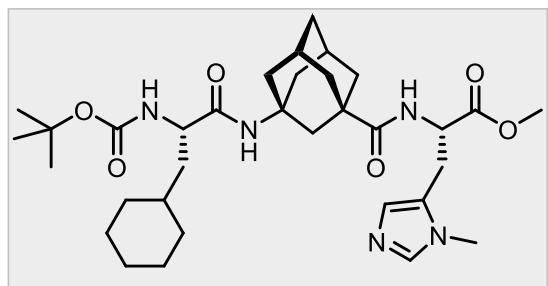
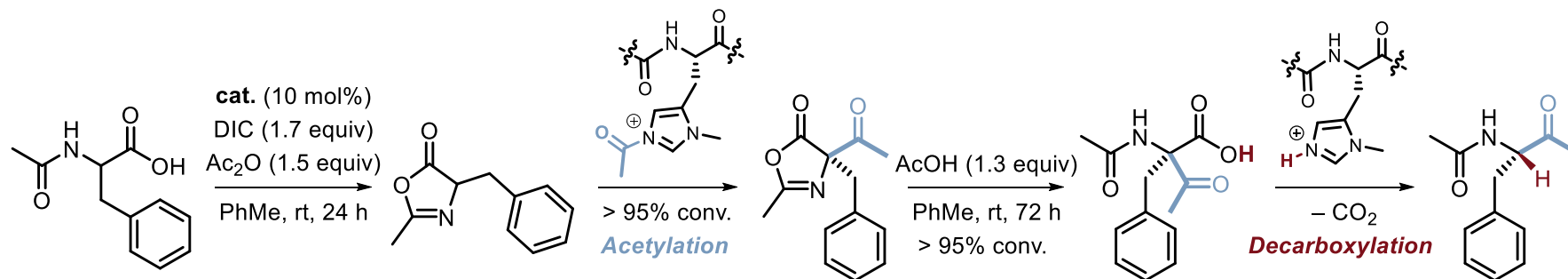


Loss of Stereochemistry

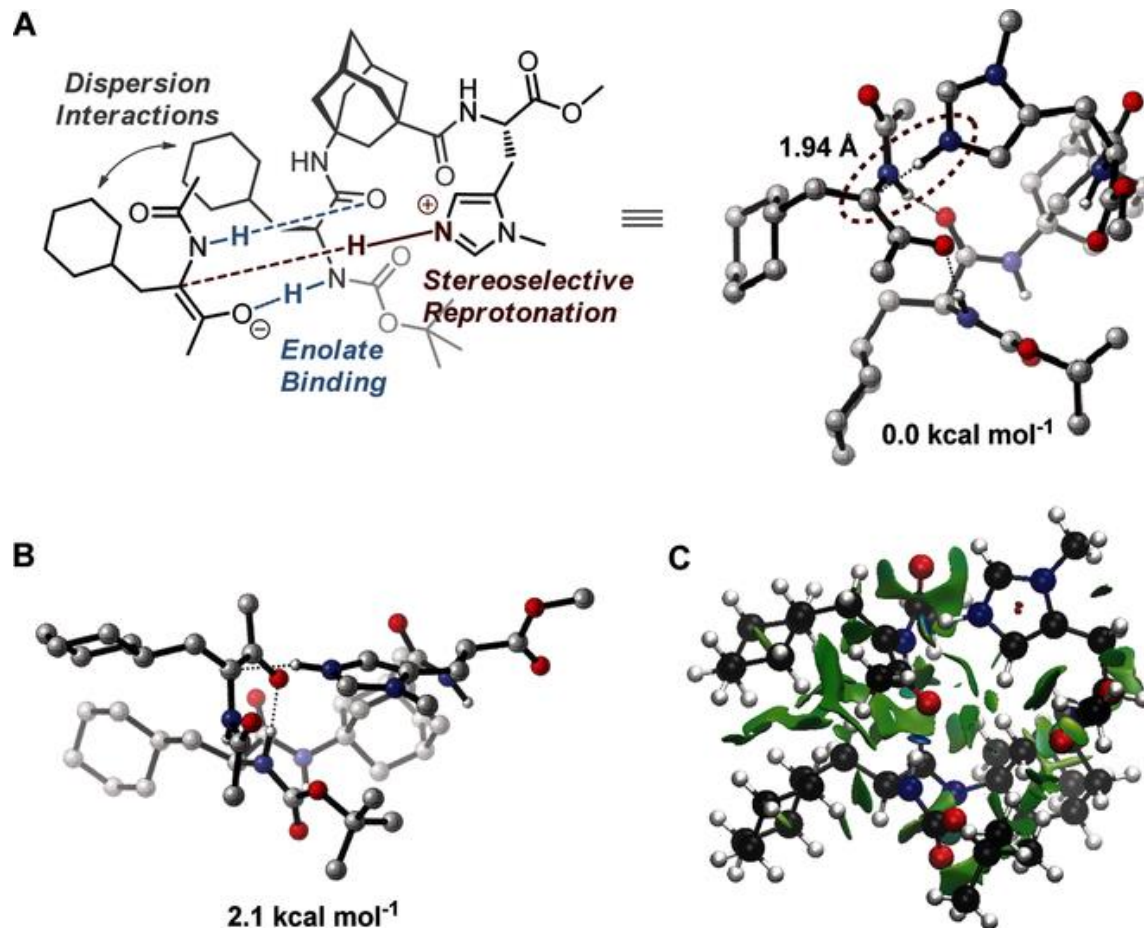


Loss of Stereochemistry

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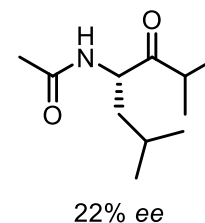
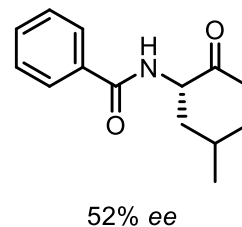
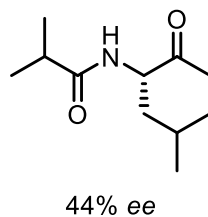
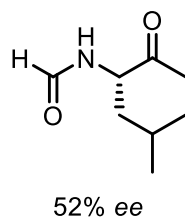
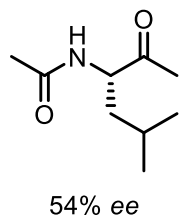
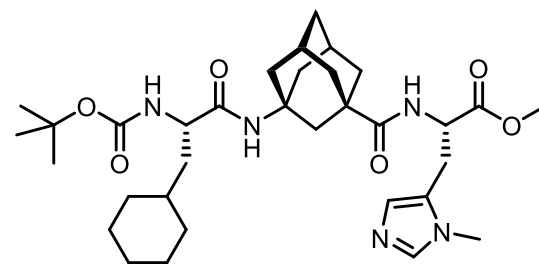
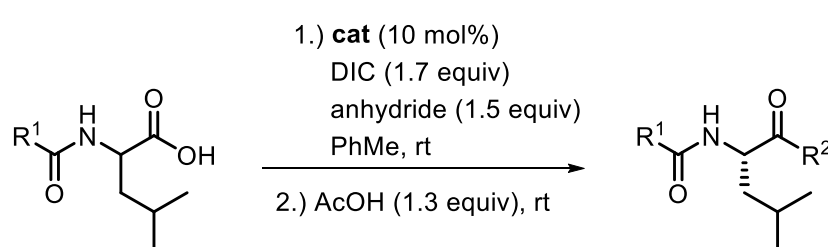
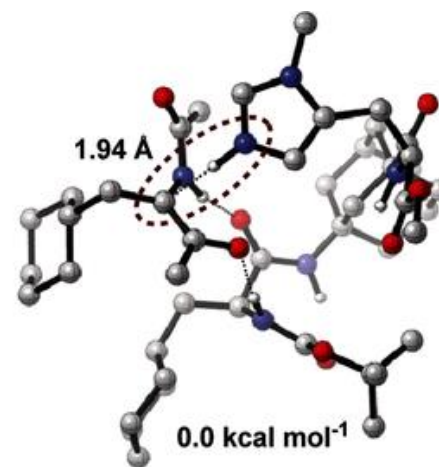
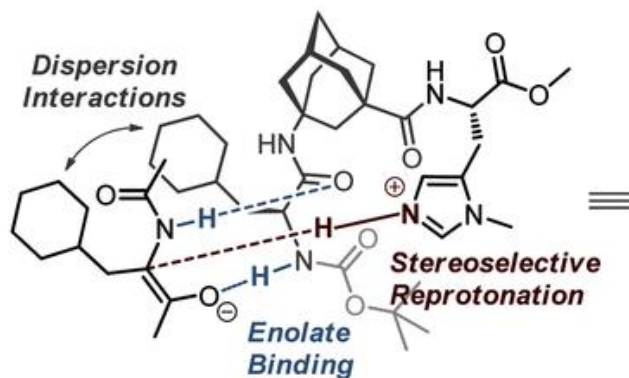


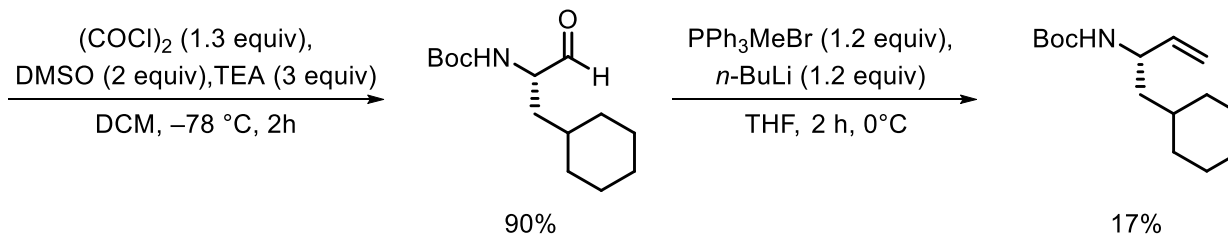
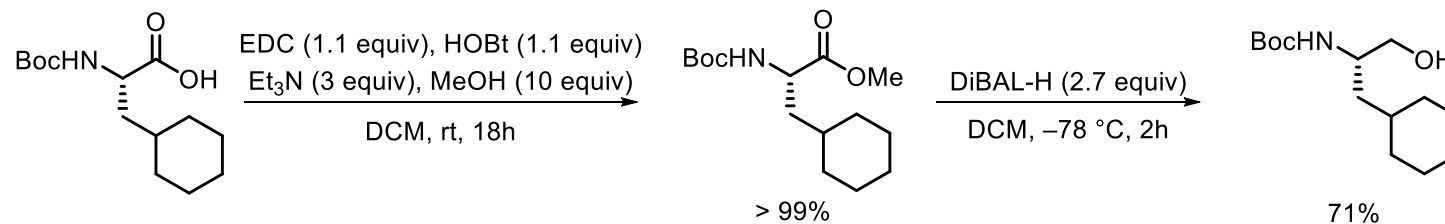
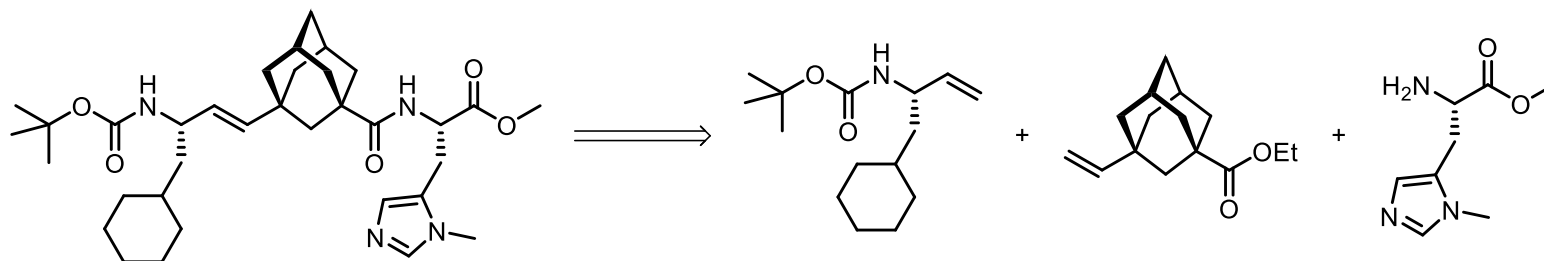
Mechanistic Proposal for Stereoinduction

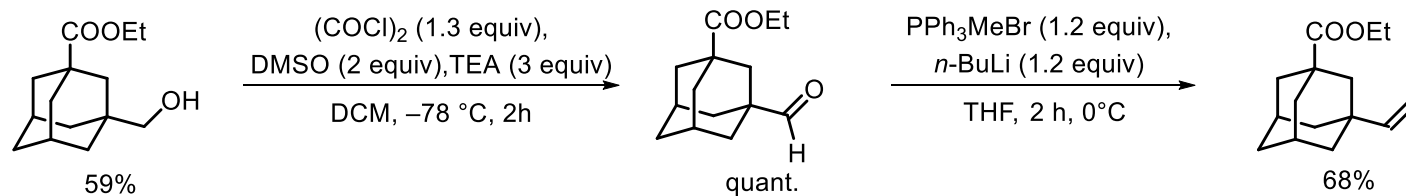
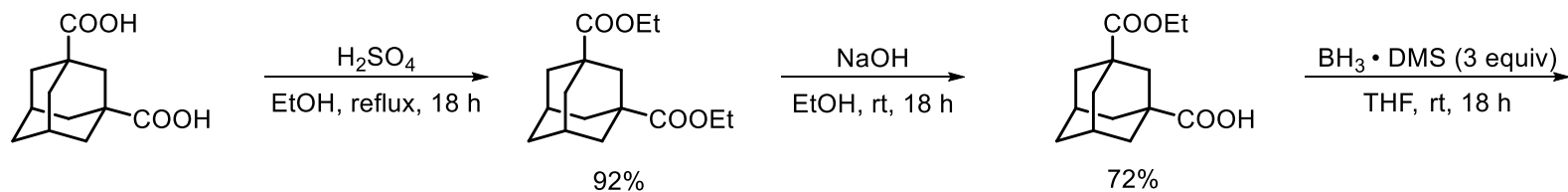
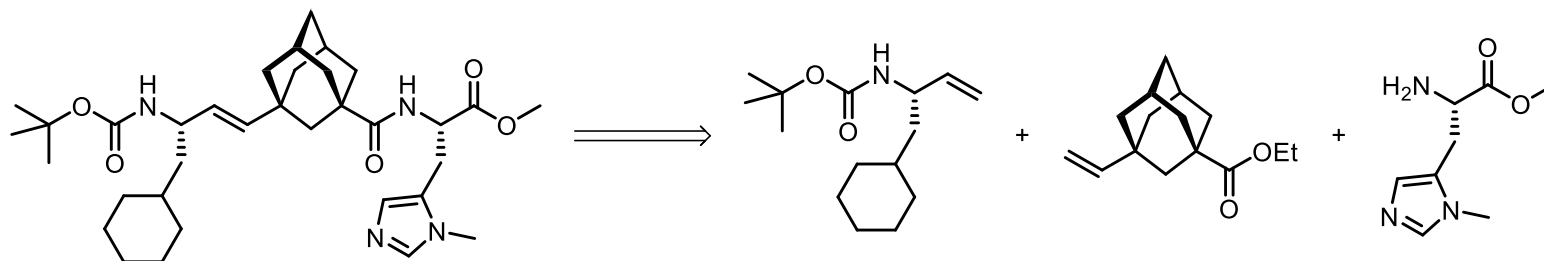


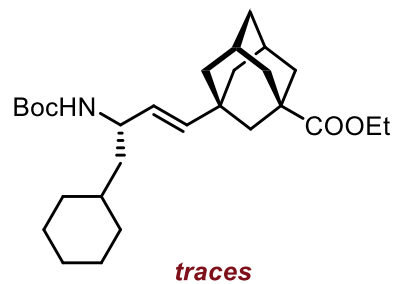
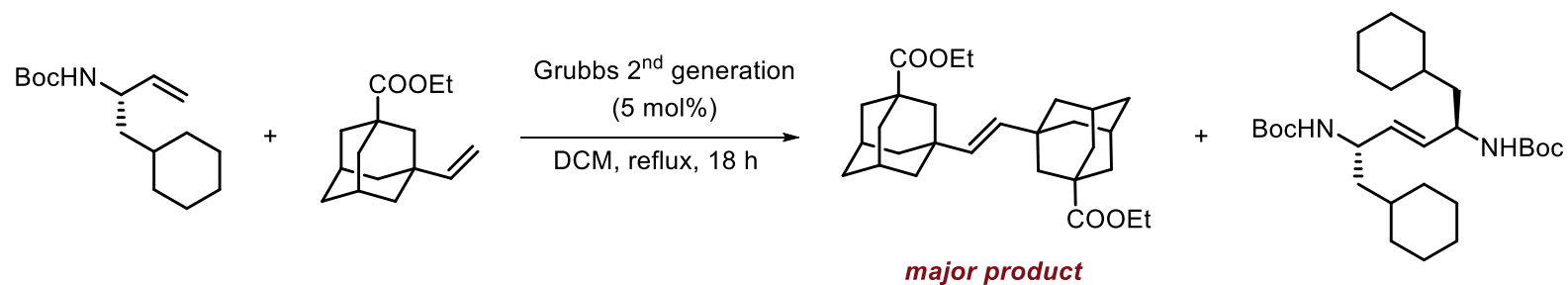
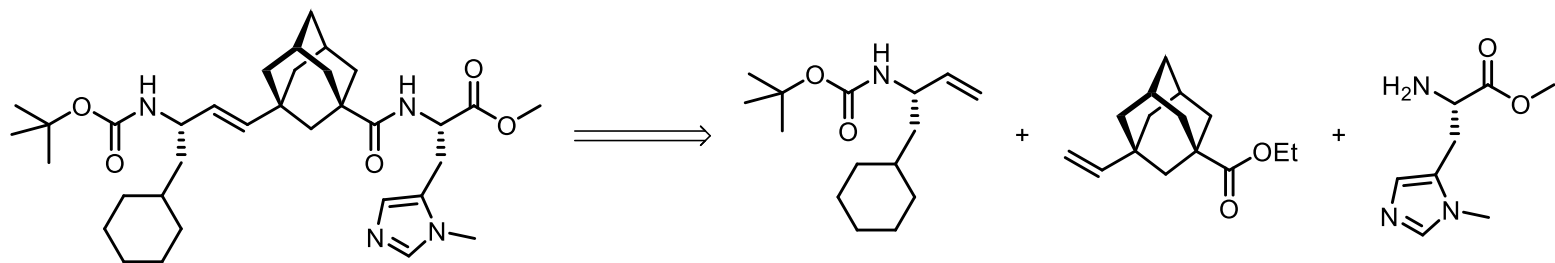
Merck Molecular Force Field (MMFF) conformer distribution; lowest lying conformers were reoptimized at B3LYP-D3(BJ)/6-31+G(d,p)

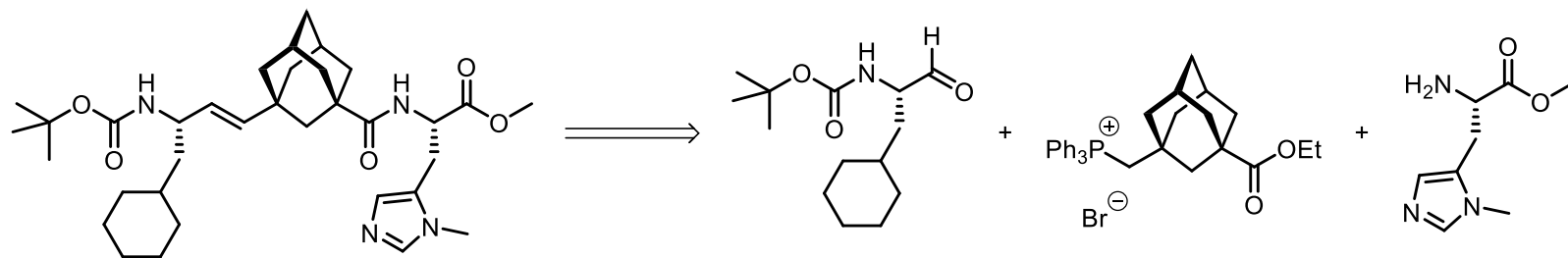
Substrate and Anhydride Variation



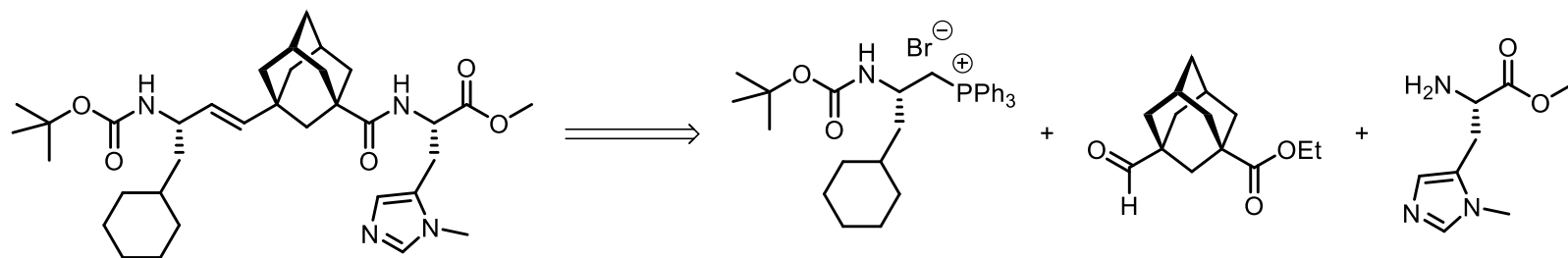




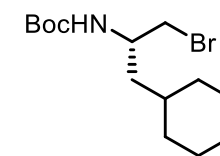
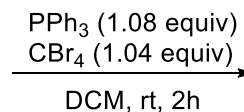
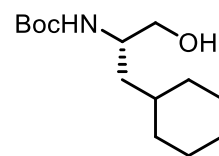
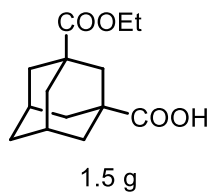




Alternative approach:

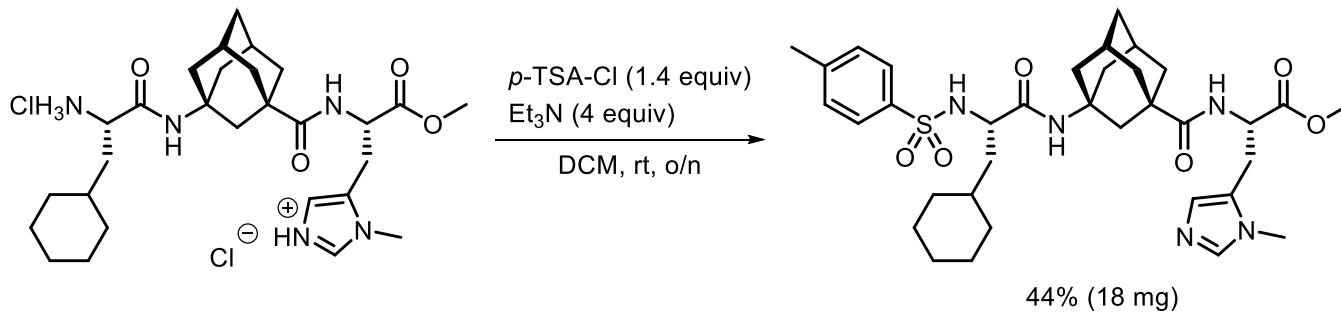
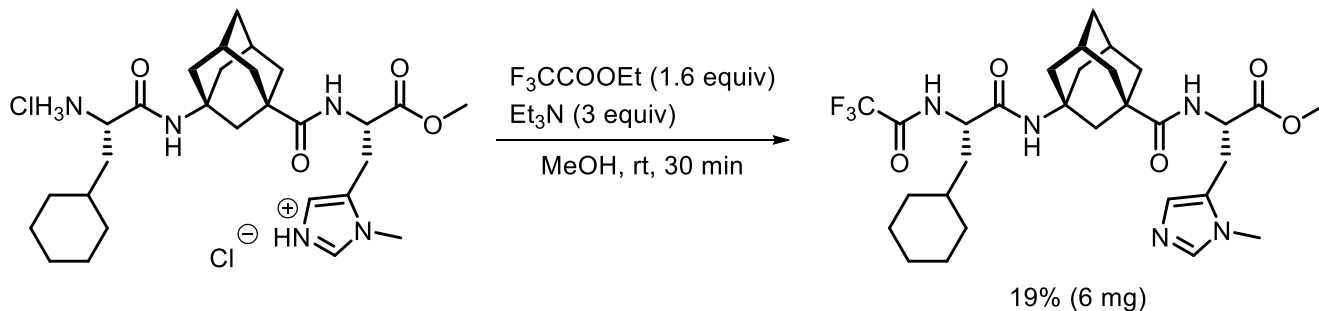
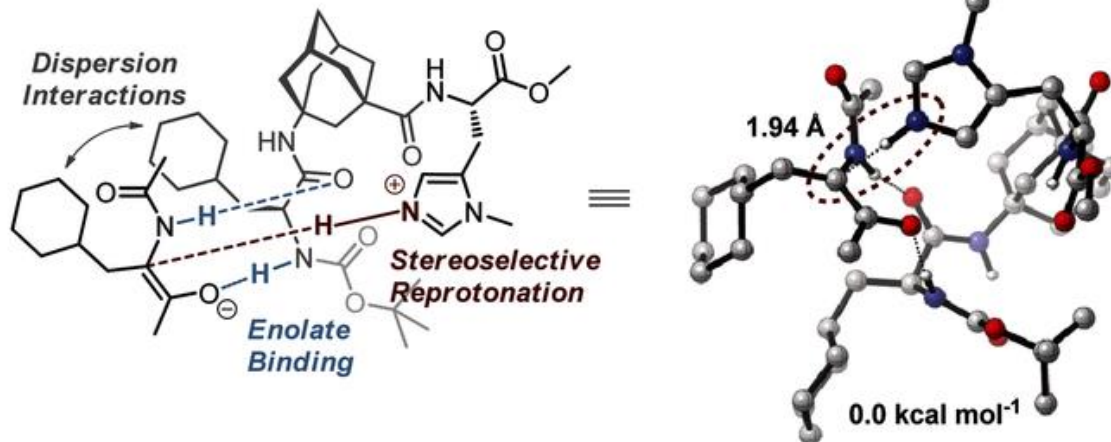


Resynthesis in progress:

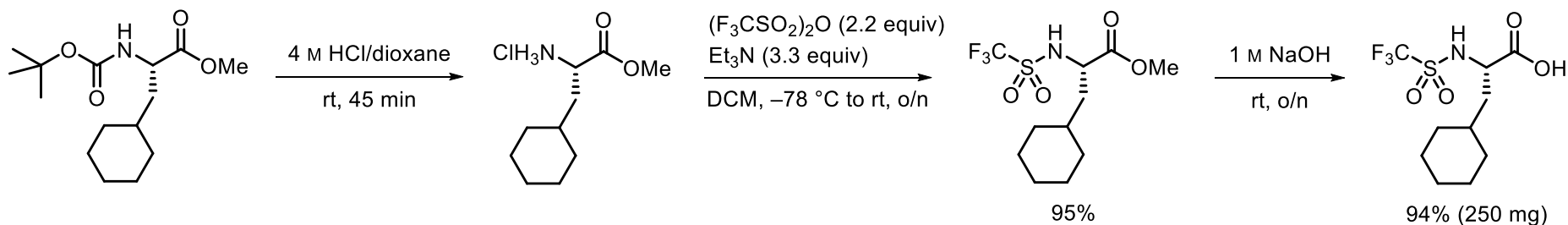
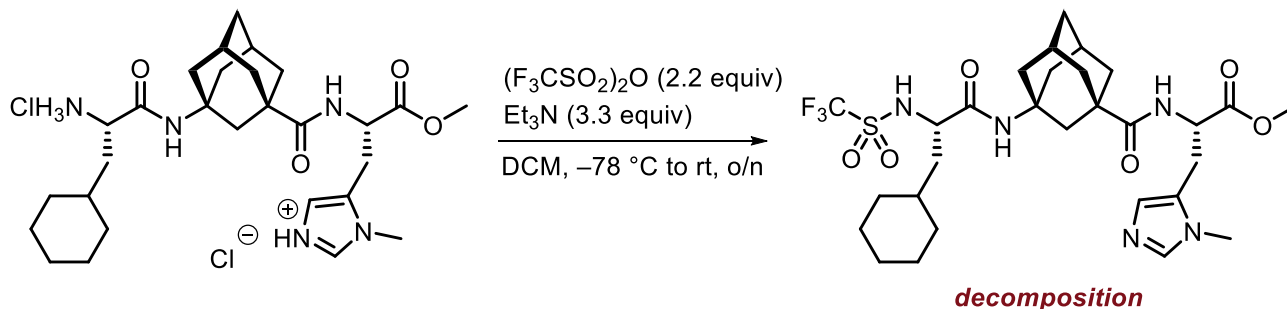


9% (20 mg)

Catalyst Variation – N-Protecting Group

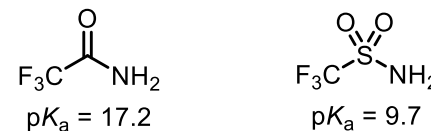
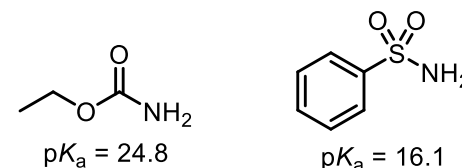


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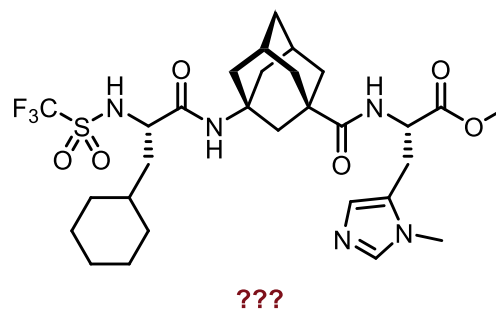
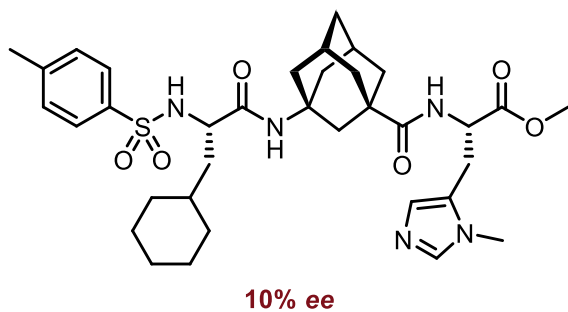
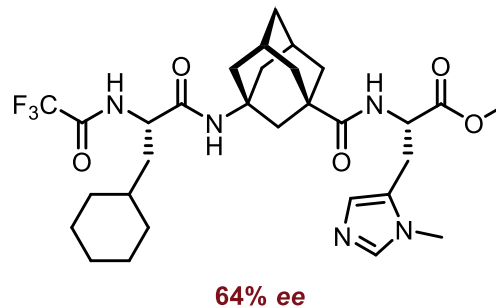
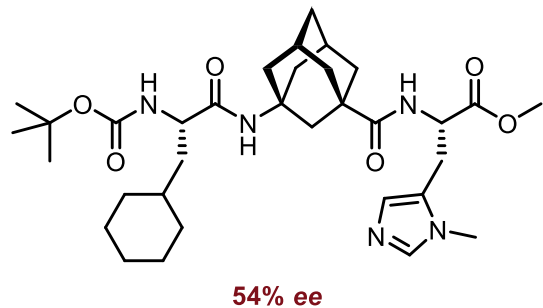
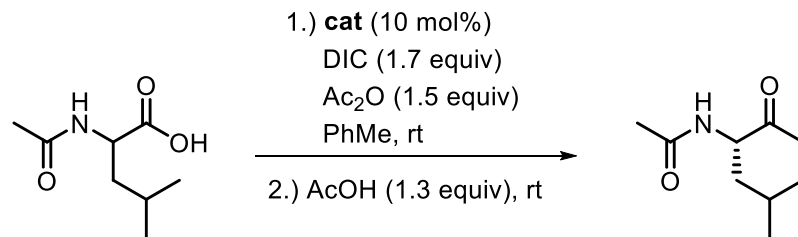


Why these protecting groups?

- Higher pK_a of N-H proton compared to the carbamate
- Stronger binding of transient enolate(?)

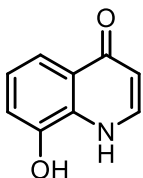


Catalyst Variation – N-Protecting Group





- Sophisticated computations of the transition states
- NMR studies on catalyst-product complexes
- Synthesis of enolate mimics



- Issue of *E/Z* ratio in the transient enolate?
- Reprotonation by acetic acid?
- Pmh as proton shuttle?



Prof. Dr. Peter R. Schreiner

Dr. Dennis Gerbig

André Eckhardt

Stefan Bernhardt

Steffen Wagner

B205 and B207

PRS Group

