

Massachusetts Institute of Technology

Organic Chemistry 5.512

March 1, 2006
Prof. Rick L. Danheiser

Introduction: Strategies for Stereocontrolled Synthesis

★ Thermodynamic Control

Relative energy of diastereomers determines outcome of reaction

I. What determines the relative energy of stereoisomers?

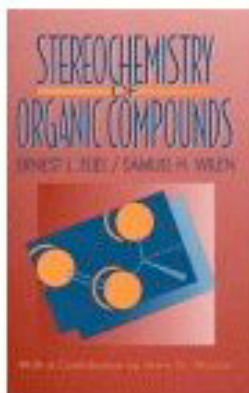
- ☆ De-stabilizing Non-bonded Repulsion
- ☆ Stabilizing Non-covalent Interactions
- ☆ Stereoelectronic Effects
 - * Deviation from optimal geometry for orbital overlap (angle strain)
 - * Destabilizing torsional interactions
 - * Stabilizing secondary orbital interactions
 - * Dipole-dipole interactions

II. Tactics for establishing thermodynamic control

Reading on Stereochemical Principles

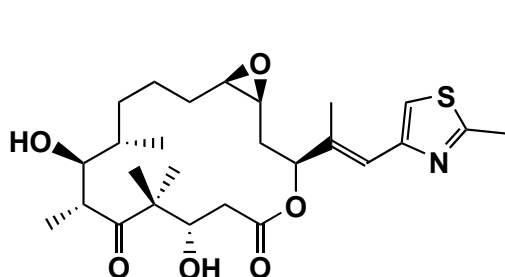
Carey and Sundberg "Advanced Organic Chemistry" Part A (2000) Chapters 2 and 3

E. L. Eliel and S. H. Wilen
"Stereochemistry of Organic
Compounds" (1994)

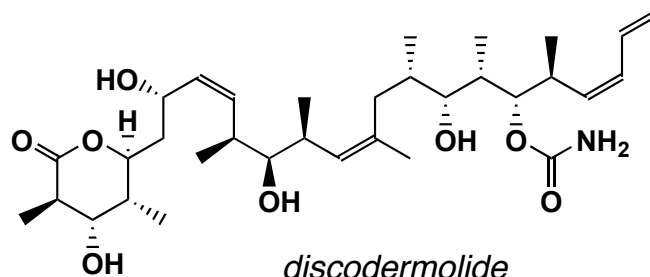


Course Syllabus

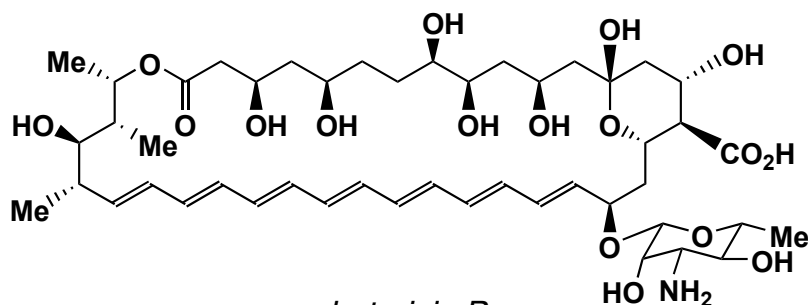
- Unit 1 Strategies for Stereocontrolled Synthesis
- Unit 2 Stereocontrolled Alkylation
- Unit 3 Stereocontrolled Conjugate Addition
- Unit 4 Stereocontrolled 1,2 Addition to C=X Bonds
- Unit 5 Addition of Allylmetals to Carbonyl Groups
- Unit 6 Stereocontrolled Aldol Reactions
- Unit 7 Stereocontrolled Carbonyl Reduction
- Unit 8 Stereocontrolled Alkene Reduction
- Unit 9 Stereocontrolled Hydroboration and Dihydroxylation
- Unit 10 Stereocontrolled Epoxidation



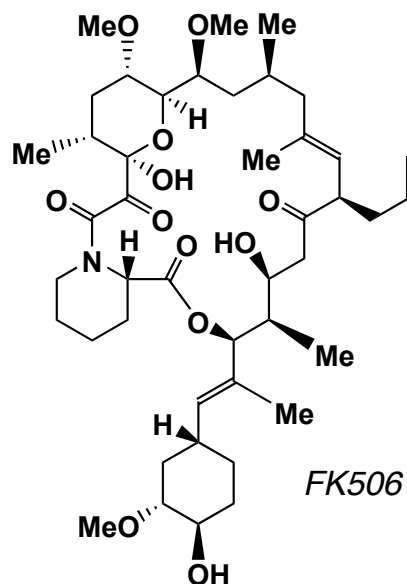
epothilone A



discodermolide



amphotericin B



FK506