

Massachusetts Institute of Technology

Organic Chemistry 5.512

March 2, 2005
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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

II. Tactics for establishing thermodynamic control

★ Kinetic Control

Relative energy of diastereomeric transition states determines outcome

☆ Substrate Control

- * Steric Approach Control
- * Stereoelectronic Control
- * Internal Stereodirection

☆ Reagent Control

- * Achiral Substrate: enantiotopic face selectivity
- * Achiral Substrate: enantiotopic group selectivity
- * Chiral Substrate: double asymmetric synthesis

☆ Dynamic Kinetic Resolution