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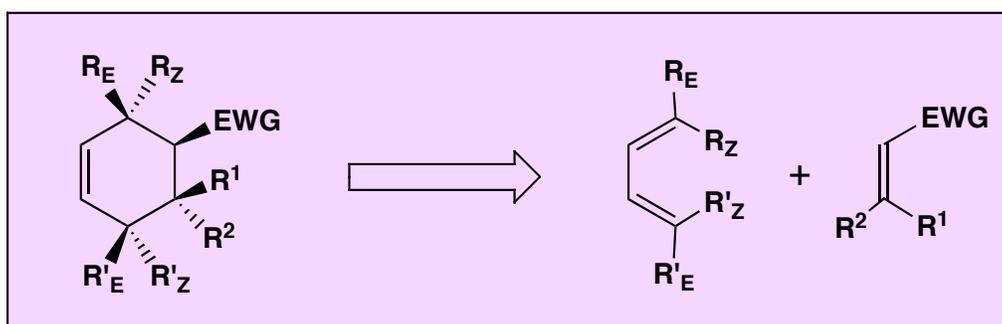
5.37 Introduction to Organic Synthesis Laboratory
Spring 2009

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Massachusetts Institute of Technology
Organic Chemistry 5.37

April 18, 2008
Prof. Rick L. Danheiser

Lecture 2
Introduction to Organic Synthesis
The Diels–Alder Reaction, Part II



Otto Diels

Our results will play a role not only in the discussion of theoretically interesting questions . . . but probably also will yield greater significance in a practical sense. Thus it appears to us that the possibility of synthesis of complex compounds related to or identical with natural products such as terpenes, sesquiterpenes, perhaps also alkaloids, has been moved to the near prospect. We explicitly reserve for ourselves the application of the reaction discovered by us to the solution of such problems.

Otto Diels and Kurt Alder *Justus Liebigs Annalen der Chemie* **460**, 98 (1928)

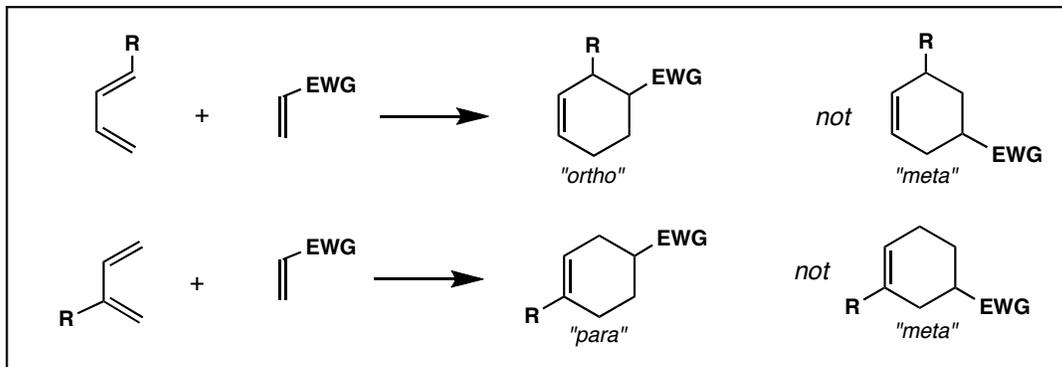


Kurt Alder

For Additional Reading

- (1) "Advanced Organic Chemistry, Part A: Structure and Mechanisms", Fifth Edition, by F. A. Carey and R. J. Sundberg, Springer, 2007, Chapter 10 ("Concerted Pericyclic Reactions"), pp 833-873.
- (2) "Advanced Organic Chemistry, Part B: Reactions and Synthesis", Fifth Edition, by F. A. Carey and R. J. Sundberg, Springer, 2007, Chapter 6 ("Concerted Cycloadditions, Unimolecular Rearrangements, and Thermal Eliminations"), pp 473-526.
- (3) "Organic Chemistry" by J. Clayden, N. Greeves, S. Warren, and P. Wothers, Oxford University Press, 2001, Chapter 35 ("Pericyclic Reactions I: Cycloadditions"), pp 905-924 and Chapter 45 ("Asymmetric Synthesis"), pp 1219-1232.

Regiochemical Course of the Diels-Alder Reaction: *The "Ortho-Para Rule"*



Stereochemical Course of the Diels-Alder Reaction

Intrinsic Stereoselectivity

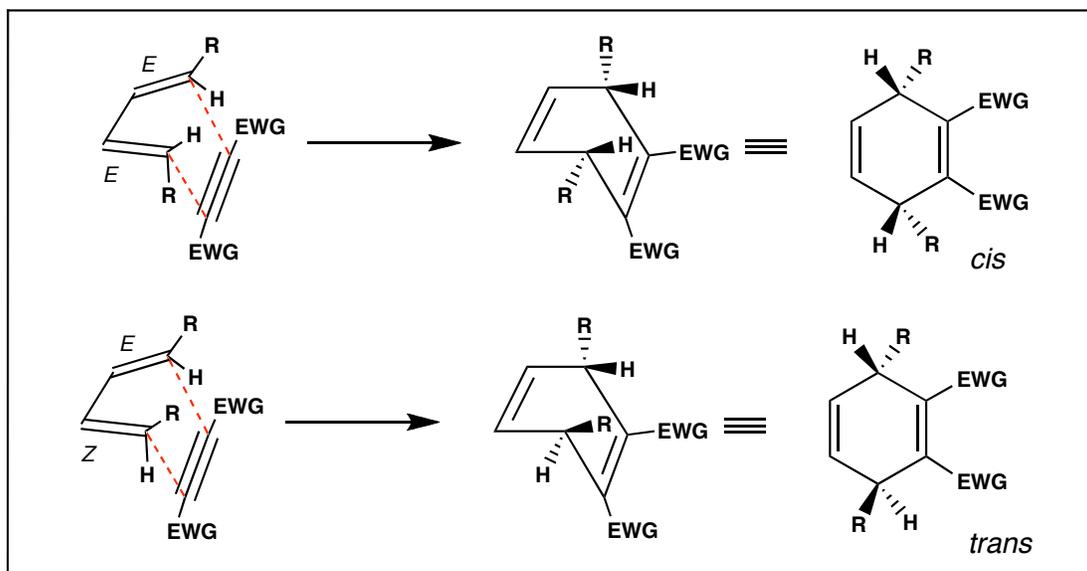
- ★ Suprafacial with respect to the diene
- ★ Suprafacial with respect to the dienophile
- ★ Alder endo rule

Asymmetric Induction

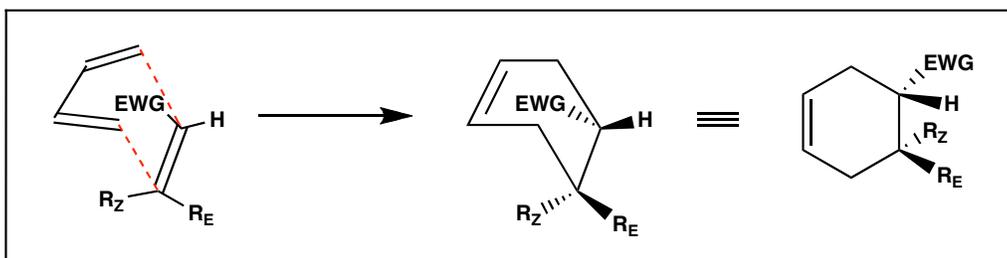
- ★ Substrate control by chiral dienophiles
- ★ Substrate control by chiral dienes
- ★ Stereocontrol via chiral auxiliaries

Catalytic Asymmetric Cycloadditions

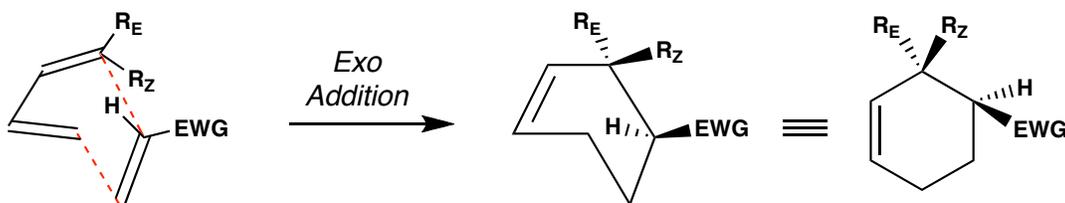
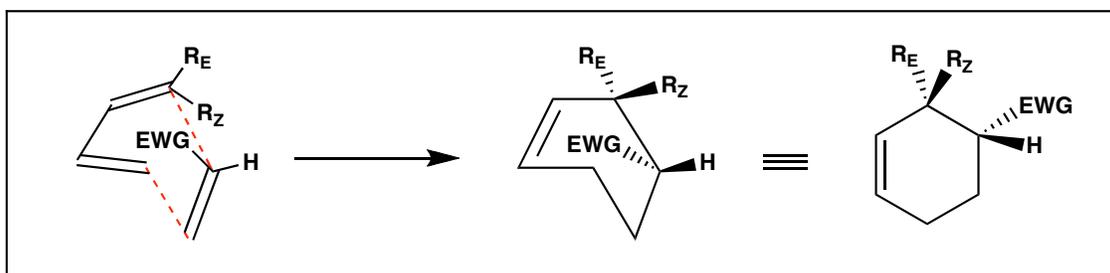
Stereochemical Course of the Diels-Alder Reaction: *Suprafacial with respect to the diene component*



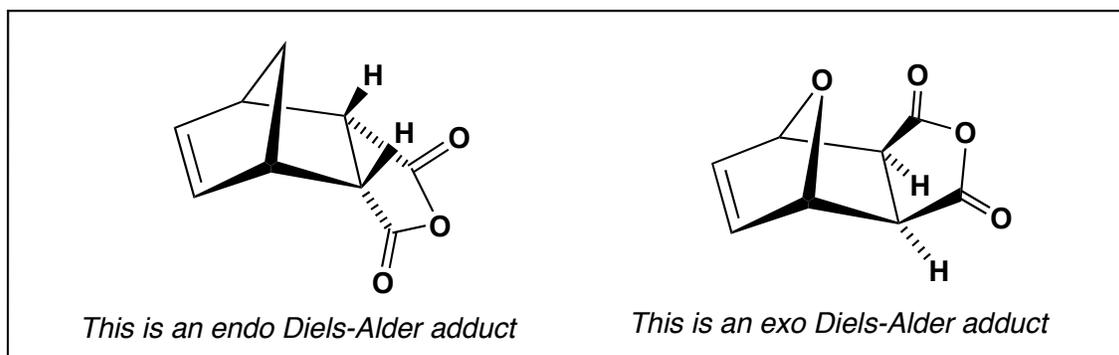
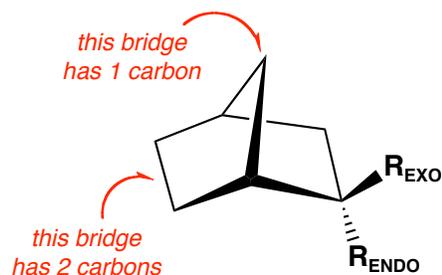
**Stereochemical Course of the Diels-Alder Reaction:
Suprafacial with respect to the Dienophile Component**



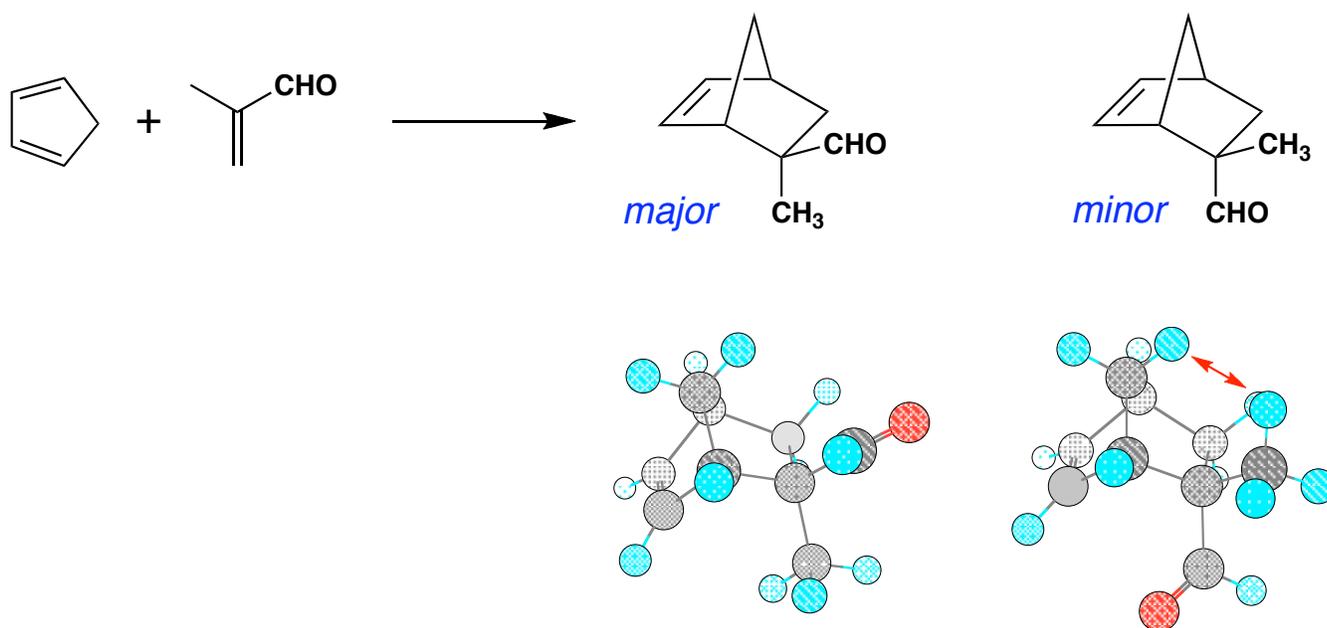
Stereochemical Course of the Diels-Alder Reaction: *The Alder Endo Rule*



The term "**endo**" originates in the terminology used to describe the stereochemistry of substituents on bicyclic ring systems. A substituent is said to be **endo** when it is *trans* to the smaller of the two bridges; an **exo** substituent is *cis* to the smaller bridge.



Steric vs. Stereoelectronic Effects in Determining Endo Selectivity



Intrinsic Stereoselectivity: Examples

Predict the major Diels-Alder cycloadduct formed in the following reactions

