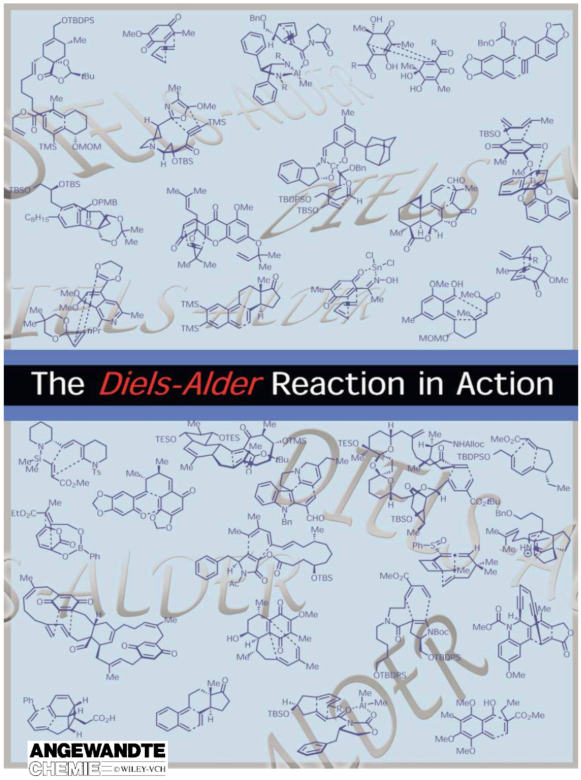
Massachusetts Institute of Technology

Organic Chemistry 5.511

October 5, 2007
Prof. Rick L. Danheiser

Unit 1

Introduction to Strategies for the Synthesis of Complex Molecules



The Diels–Alder Reaction

If one chemical reaction had to be selected from all those in the repertoire of synthetic organic chemists as the most useful and powerful synthetic construction, it was clear by 1970 that the Diels-Alder reaction would be the logical choice. Its application not only leads to a strong increase in molecular complexity (molecular size, topology, stereochemistry, functionality, and appendages), but also can result in structures that lend themselves to additional amplification of complexity by the use of other powerful synthetic reactions.

E. J. Corey *Angew. Chem. Int. Ed.* **2002**, *41*, 1650

Reading Assignment

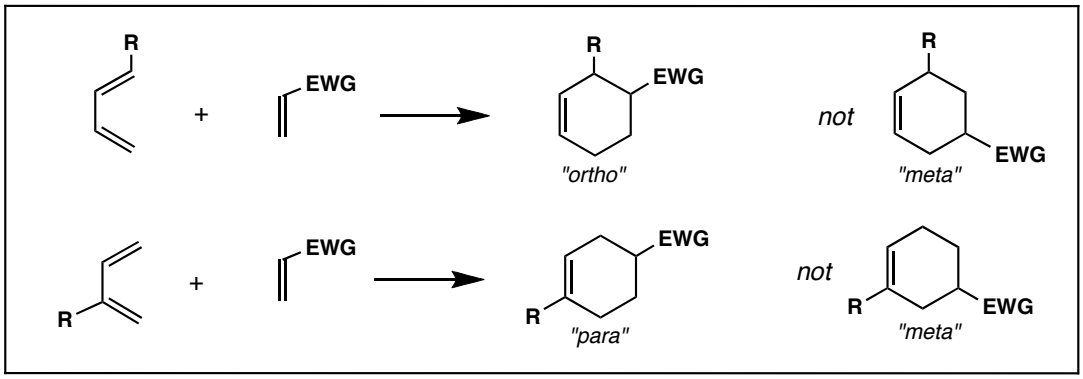
Background: Clayden et al. Chapter 35

Carey and Sundberg Part B, Chapter 6, Sections 6.1.1- 6.1.4 (pp 473-499)

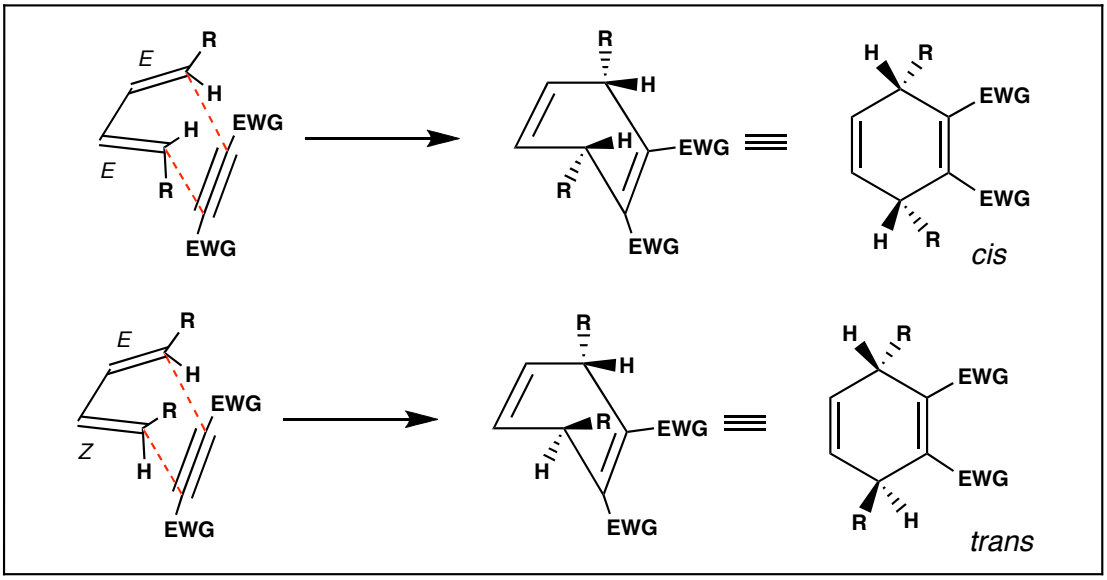
Kürti and Czakó pp 140-141

See Kürti and Czakó pp 575-576 for a listing of review articles on the Diels-Alder reaction

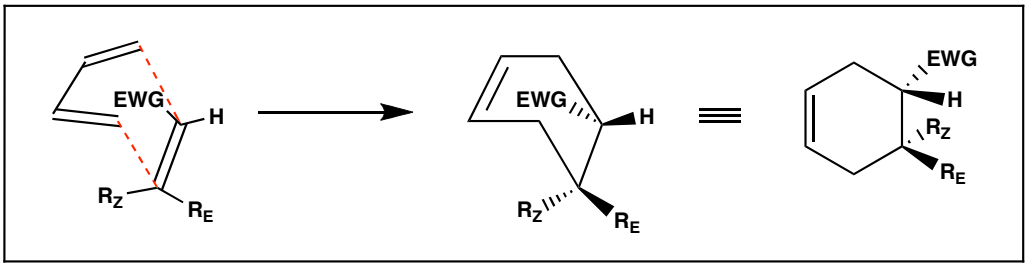
Regiochemical Course of the Diels-Alder Reaction: *The "Ortho-Para Rule"*



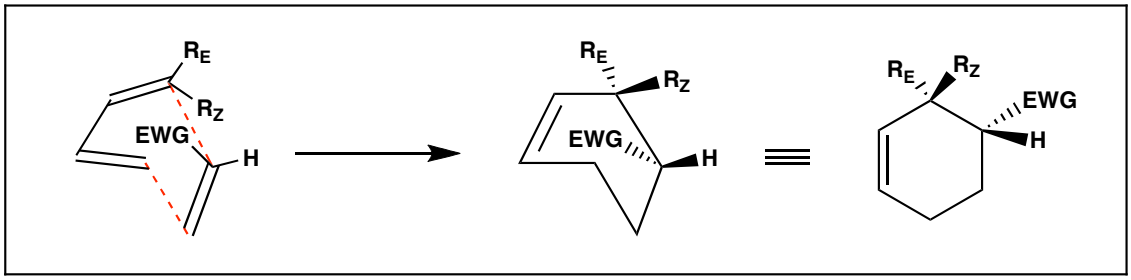
Stereochemical Course of the Diels-Alder Reaction:
Suprafacial with respect to the diene component



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



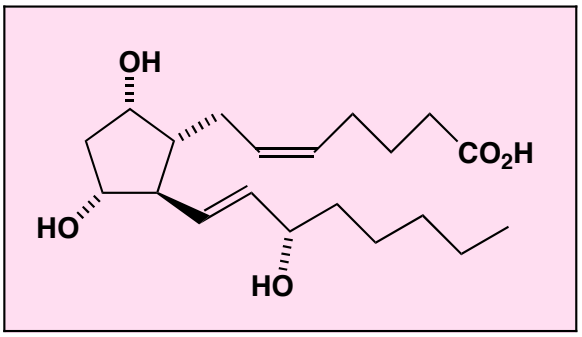
Stereochemical Course of the Diels-Alder Reaction: *The Alder Endo Rule*



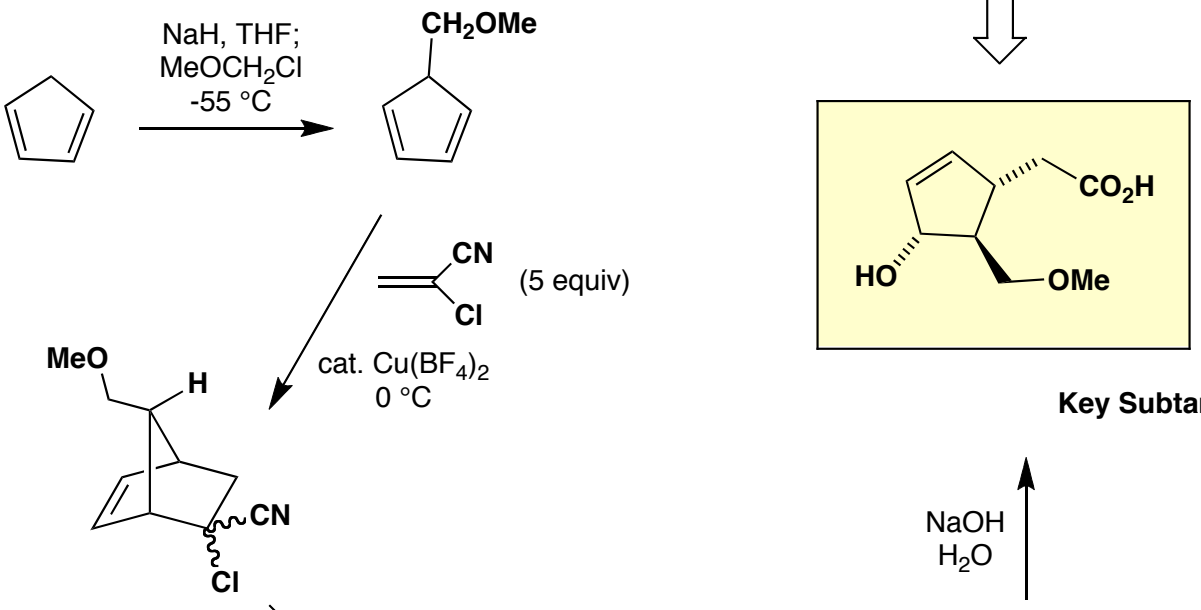
Case Study

Total Synthesis of Prostaglandins

Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675



Prostaglandin $F_{2\alpha}$

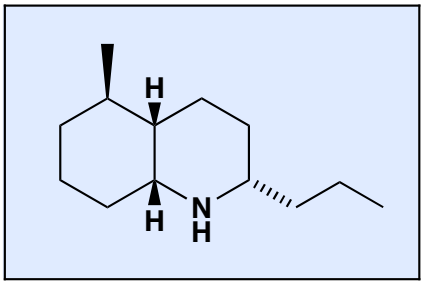


Key Subtarget

What is the mechanism of this hydrolysis? See C. S. Shiner et al. *Tetrahedron Lett.* **1983**, *24*, 5687

Case Study

Total Synthesis of *d,l*-Pumiliotoxin C
Overman, L. E.; Jessup, P. J.
J. Am. Chem. Soc. **1978**, *100*, 5179



Review of quinolizidine and indolizidiene natural products, see
Daly, J. W.; Spande, T. F.; Garraffo, H. M.
J. Nat. Prod. **2005**, *68*, 1556

Quote of the Day

"There is diminishing need for the logistically intensive multistep assaults simply because the mountains are "there". The syntheses that will warrant the greatest interest are those which convey new ideas and new chemistry arising from a willingness to explore ambitious and risky propositions. It is in the context of dreaming such dreams and, above all, in the struggle to reduce them to a "do able" state, that the power of our science, as well as its beauty, flourishes."

Samuel J. Danishefsky in
Tetrahedron **1997**, *53*, 8689