

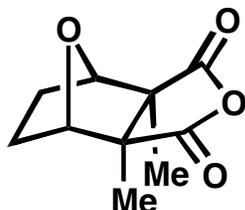
Organic Chemistry 5.13

October 16, 18, and 20, 2006
 Prof. Timothy F. Jamison

Notes for Lectures 15, 16, and 17

Cycloaddition Reactions

Molecule of the Day
cantharidin



Cantharidin is a powerful **irritant** isolated from *Cantharis vesicatoria*, a.k.a. the "blistering beetle" or "Spanish fly", and is found in the eponymous, alleged aphrodisiac. Several chemistry research groups have prepared cantharidin by total synthesis, and in many of these a **Diels-Alder reaction** was a key step.

Cycloaddition: A pericyclic reaction in which 2 **separate** conjugated, overlapping arrays of orbitals **combine**. Cycloadditions proceed by way of a **cyclic transition state**, and 2 **sigma bonds** are formed during the course of the reaction.

A **suprafacial** process ("s" in the table below) is one in which the bonds made or broken lie on the **same face** of the orbital array undergoing reaction. In an **antarafacial** process ("a"), the newly formed or broken bonds lie on **opposite faces** of the reacting orbital array.

Woodward-Hoffmann Rules for Cycloadditions

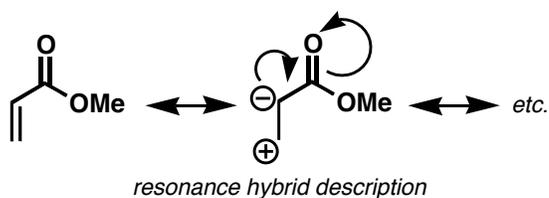
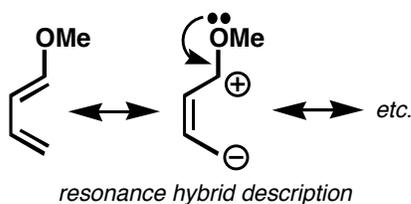
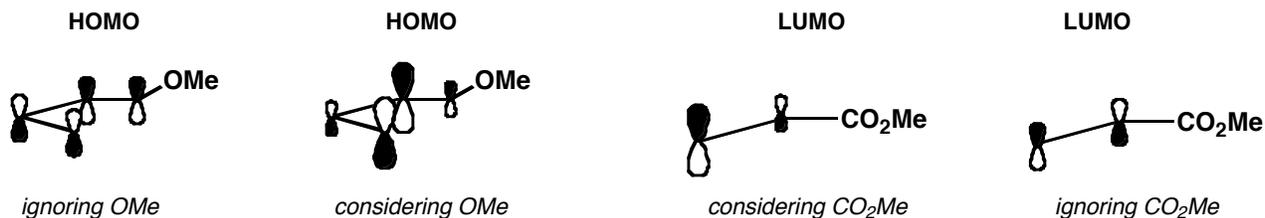
# Electrons	Stereochemical Course	
	Thermal Mode	Photochemical Mode
4n + 2	[s + s]	[s + a]
4n	[s + a]	[s + s]

Coefficients of Frontier Molecular Orbitals

FMO Analysis of the "Ortho-Para Rule" and the "Alder Endo Rule"

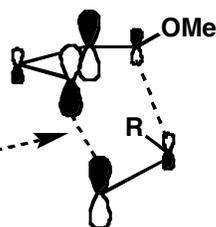
For an in-depth discussion, see

I. Fleming, "Frontier Molecular Orbitals and Organic Chemical Reactions," Wiley, 1976, pp. 121-181.

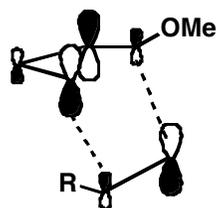


• Regioselectivity?
"ortho-para rule"

overlap maximized



vs.

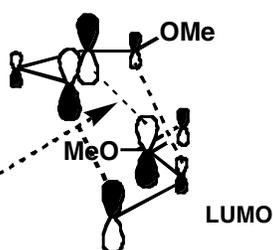


Note: changes to coefficients of anti-bonding orbitals are **opposite** those seen in bonding orbitals.

• Diastereoselectivity?
"Alder endo rule"

consider orbitals of CO₂Me

secondary orbital interaction



vs.

