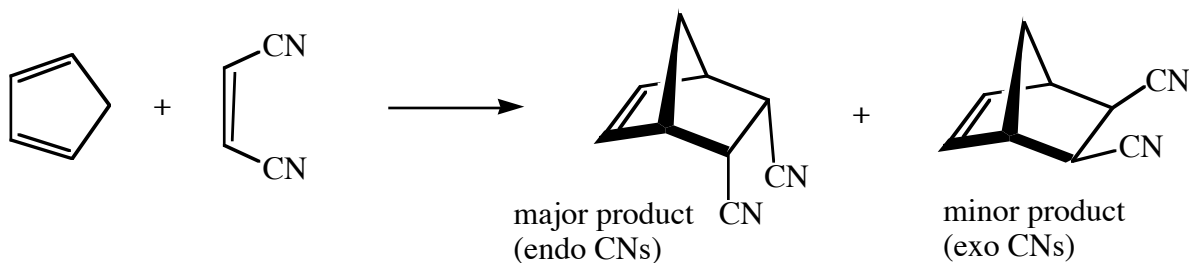


*Lecture outline*

**Diels-Alder Reaction (cont'd)**

4. "*Endo effect*" — substituents conjugated with the reacting  $\pi$ -bond of the dienophile tend to end up in the "endo" position of a bicyclic ring system.

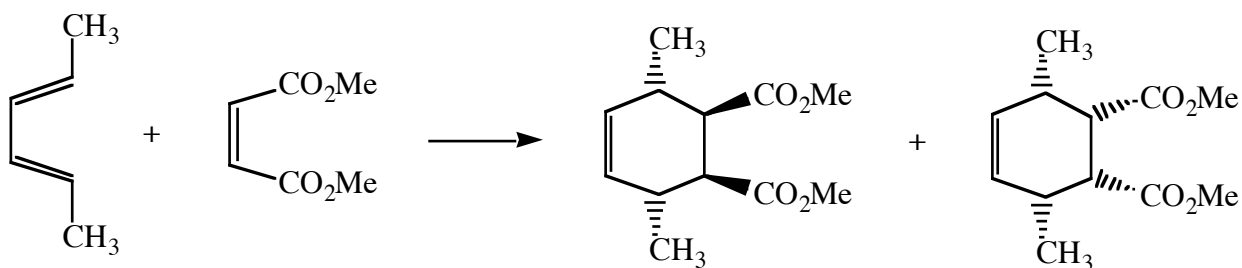
This is because the transition state leading to this product gains a bit of extra stabilization from the interaction of the substituent with the diene p-bond.



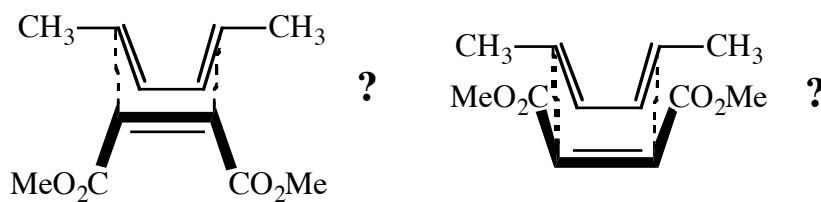
With the two reactants approaching each other in the orientation that leads to the *endo* product, sketch the frontier orbitals and find the extra stabilizing interaction. (Note that for *exo* approach, no secondary interaction, good or bad, is possible.)

This effect also controls stereochemistry in reactions of acyclic dienes, but, of course, the term "endo" has no meaning in describing the stereochemistry of the monocyclic products — we use cis/trans for these.

Decide which is the major product in the following case by sketching the favored "endo" transition state and paying careful attention to stereochemistry.

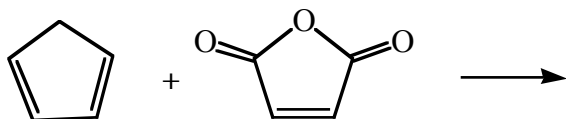


Two directions of approach are possible — which is "endo", and which is "exo"? which one leads to which product?



The endo effect is kinetic — it affects the energies of the transition states leading to the products.

Cyclopentadiene and maleic anhydride react to form two products with exo and endo stereochemistry. Draw them in the space below.



The *endo* product is the major one when the reaction is carried out at room temperature, but when the reaction is carried out at high temperature (ca. 200°C), the *exo* is found to be the major product. What's up with that?

## 5. Electronic requirements — rxn works best when:

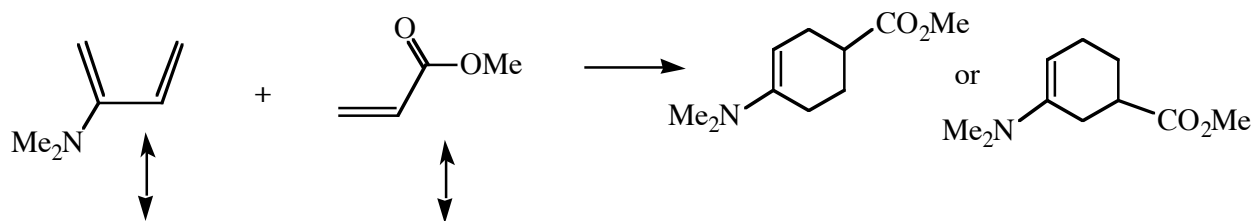
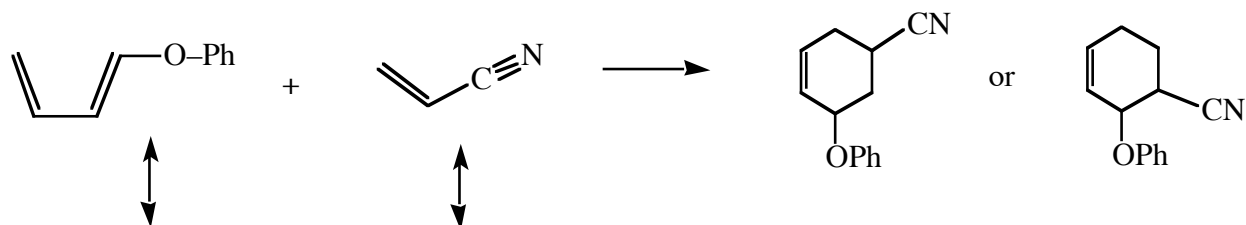
(1) *dienophile* has  $e^-$ -withdrawing substituents like  $-\text{CN}$ ,  $-\text{CO}_2\text{R}$ , etc, giving its  $\pi$ -bond a  $\delta^+$  charge (i.e. making it *electrophilic*) and/or *diene* has  $e^-$ -donating substituents like  $-\text{OR}$ ,  $-\text{NR}_2$ , etc, giving its  $\pi$ -bond a  $\delta^-$  charge (i.e., making it *nucleophilic*). Reaction of an electron-rich diene and an electron-poor dienophile is a "normal electron demand" D-A rxn;

or (2) the other way around — dienophile is electron-rich, and diene is electron-poor — a less common "inverse electron demand" D-A rxn;

or (3) either diene or dienophile has unsaturated substituents like  $-\text{CH}=\text{CH}_2$ ,  $-\text{Ph}$ , etc, in conjugation with the reacting  $\pi$ -bonds.

In addition, substituents — often control the regiochemistry of the reaction —

We can often predict which of two regioisomeric products should be favored by looking at the partial charges created on the reacting Cs by  $e^-$ -withdrawing and by  $e^-$ -donating substituents. In each case below, predict which is the major product by (1) drawing the best zwitterionic (i.e. charge separated) resonance structure for each reactant, and (2) recognizing that attraction between + and - charges is a good thing.



A more robust, theoretically meaningful, and general way to understand D-A regiochemistry is to examine the effects of substituents on the energies and p-orbital coefficients of the HOMO and LUMO of the reactants. We'll do this next time.