

## Bonding, Cycloadditions, and Terpene Mechanisms

### Section Agenda

- 1) Random Stuff, Decide on Better Time for Office Hours
- 2) Return Problem Set 1
- 3) Handout: "How to Win Chem 30"
- 4) Handout: Section 2 (this one)
- 5) Handout: Section 2 Practice Problem Set

### Announcements

#### New Office Hours

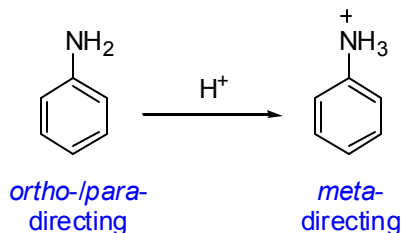
- Thursdays, 3-4PM and 8-9PM in the Bauer Lobby

#### Correction

- In the Section 1 handout distributed last week, there is an error in the section on the anomeric effect. The 3D Lewis structures (chair drawings) were mismatched with their 2D counterparts (hexagons with dashes and wedges).
- If you catch any typos or errors, drop me an e-mail so I can stop error proliferation by posting corrected versions of the handouts on the course Web site.

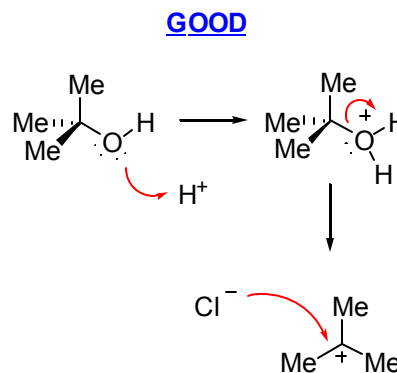
#### Problem Set 1 Fallout

- Anilines are basic ( $pK_a$  for conj. acid. = 4), so in acidic solutions, these compounds will be protonated. While nitrogen substituents generally activate an aromatic ring by a resonance effect, they are deactivating when protonated.

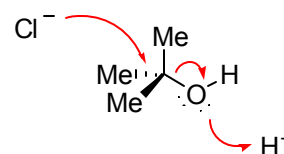


- Simple proton transfers are fast compared to electrophilic aromatic substitution reactions. In general, proton transfers are among the fastest reactions.

- Unlike how you're taught in Chem 27, do not draw overly abbreviated mechanisms. When a reaction occurs stepwise, you should draw out the expected intermediates and indicate any important considerations which factor into the mechanism (such as resonance structures of reactive intermediates).



**NOT GOOD**



- Problem sets are graded in whole points, so small/stupid/careless errors will cost you big time.

## Building Molecular Orbitals (MOs)

- I'm bumping this up from material that appears later in the semester (pericyclic reactions) because you're getting MOs crammed down your throats now. This is a little shorter version of last week's handout and includes a pictorial example on the next page.

### Simple Rules

- Atomic orbitals must overlap if they are to interact to form a set of molecular orbitals. There are no exceptions—orthogonal orbitals will not interact.
- You will get  $n$  molecular orbitals (MOs) for every  $n$  atomic orbitals (AOs) that interact.
- The most stable MOs have the most bonding character. The highest energy MOs have the most antibonding character. In the same  $\pi$  system, the energy of an MO is directly proportional to the number of nodes. Thus, as the number of nodes increases, the antibonding character increases and the orbital lies higher-in-energy.
- The electron density at an atom is equal to the square of the MO's coefficient at that atom. Locations with bigger coefficients are depicted by drawing bigger orbital lobes.
- The + and – designations, also shown as green and blue, have *nothing* to do with charge. They are designations for the sign of that orbital's wavefunction. When orbitals of the same wavesign interact, there is constructive interference resulting in a bonding interaction. When orbitals of the opposite wavesign interact, there is destructive interference resulting in an antibonding interaction.
- Nodes are locations in the system where the bonding interactions are completely cancelled by antibonding interactions. Molecular orbitals have zero electron density at nodes. Reactions will not occur at these locations.
- Molecular orbitals for equivalent atoms are symmetric. Note how the MOs below either have a mirror plane of symmetry (a "symmetric" MO = **S**) or a  $C_2$  axis of symmetry (an "antisymmetric" MO = **A**).
- Note patterns in MO diagrams to help you draw them and to figure out "shortcuts" in problem solving
  - In the lowest energy MO, all of the wavesigns are the same
  - In the highest energy MO, all of the wavesigns alternate
  - The termini alternate between having the same wavesign and opposite wavesigns
  - The number of nodes increases by one as you climb higher in energy
  - For linear systems with an odd number of AOs, some nodes will lie at atoms in the chain

### Electronic Perturbations of Molecular Orbitals

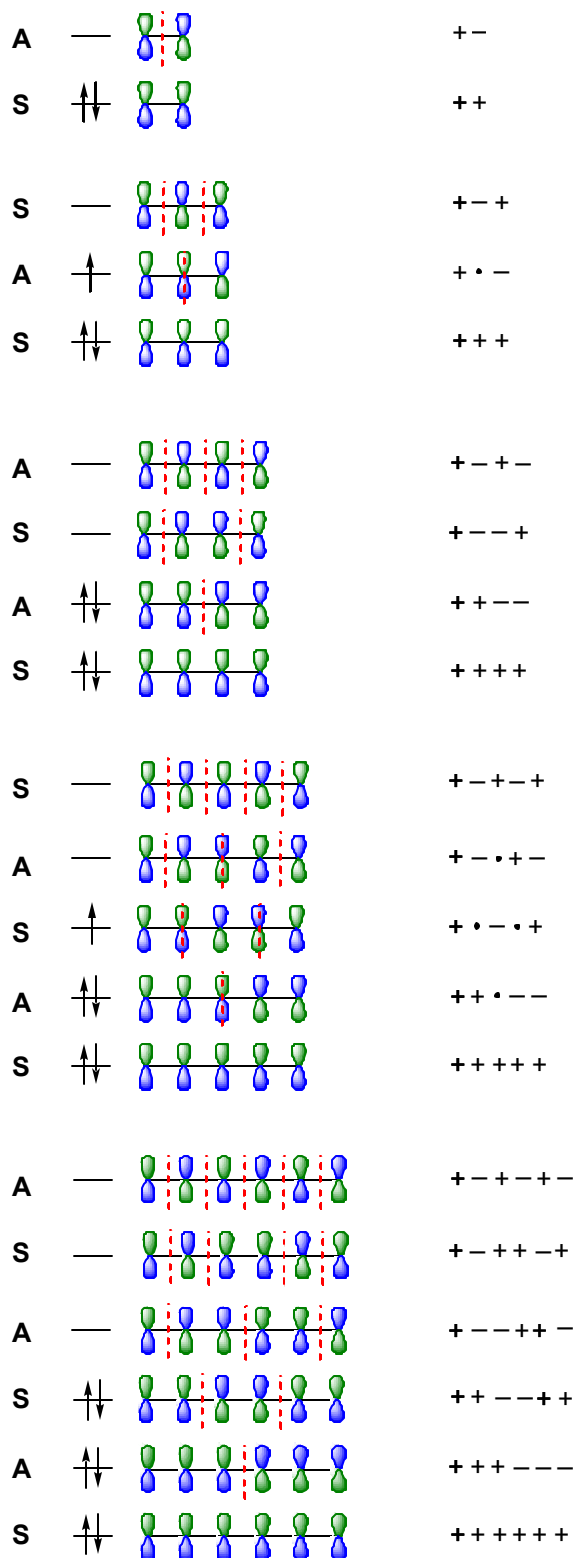
Placing electron donating groups (EDGs) or electron withdrawing groups (EWGs) on a  $\pi$  system will shift or "perturb" the relative energies of the molecular orbitals.

- EDGs will push more electron density into the  $\pi$  system and will correspondingly raise the energies of the molecular orbitals
- EWGs will pull electron density out of the  $\pi$  system and will correspondingly lower the energies of the molecular orbitals
- Lewis acids that complex with extended  $\pi$  systems also lower the energies of the MOs. These metals typically serve as catalysts by lowering the energy of a reactive LUMO such that it is more accessible.

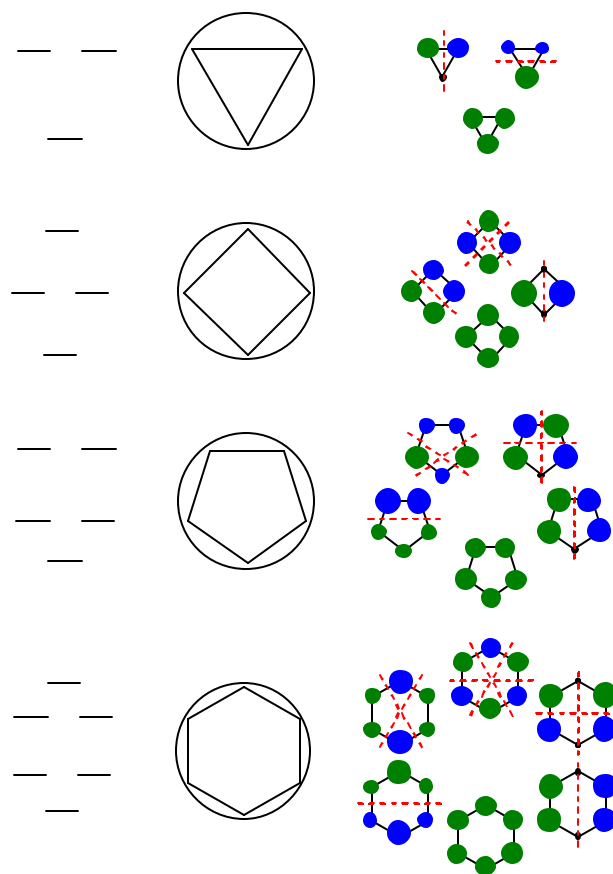
Determining which atoms will become enriched or depleted in electron density can be accomplished by using an electron pushing model.

## Graphical Depictions of Molecular Orbitals

### Linear Systems



### Cyclic Systems



### Frost Circles

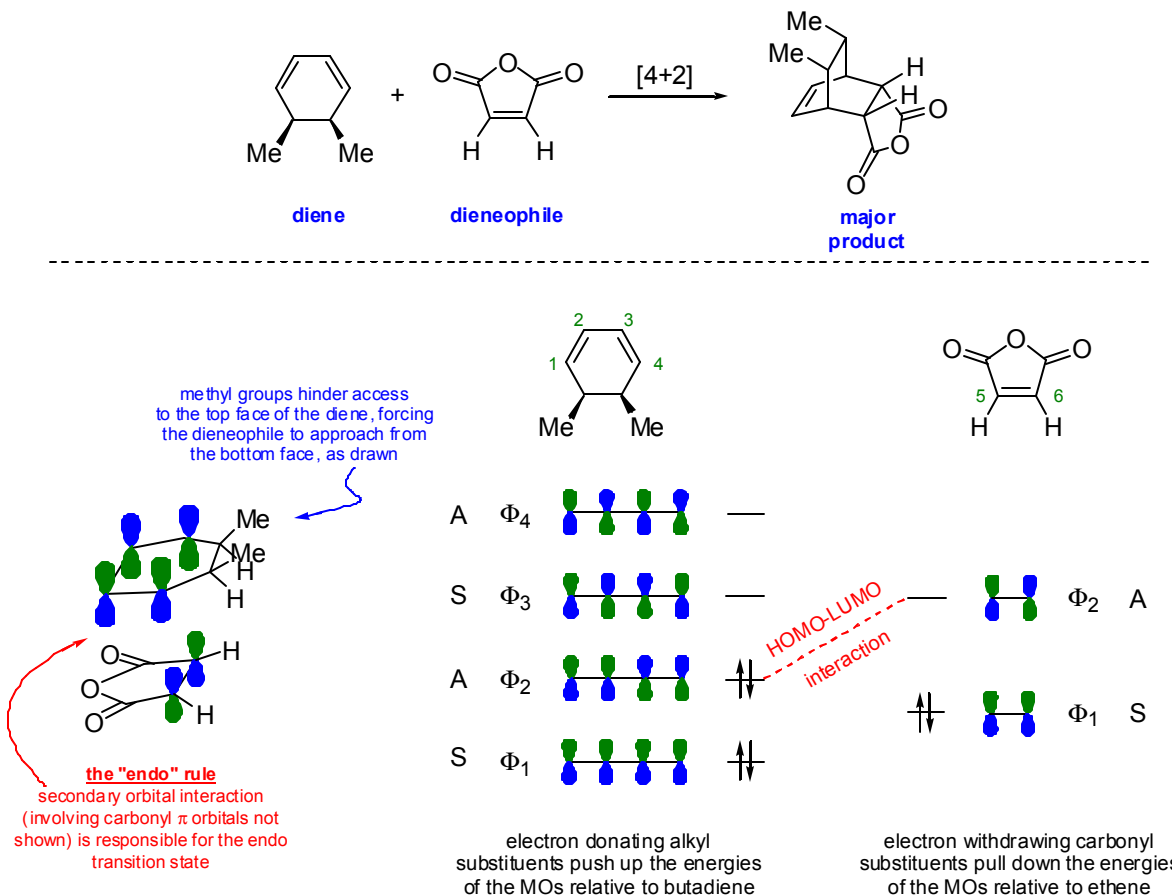
- Frost circles are the fastest method to arrive at the molecular orbitals for conjugated cyclic systems.
- You simply inscribe the polygon in a circle "vertex down," such that one of the corners touches the bottom of the circle.
- Each vertex of the polygon represents the energy level of a molecular orbital.
- For Chem 30, you need only worry about the relative position of the MOs and not the quantitative energy difference between the MOs. However, the reason Frost circles are so powerful is that they can be used to get these energies.

## Cycloaddition Reactions

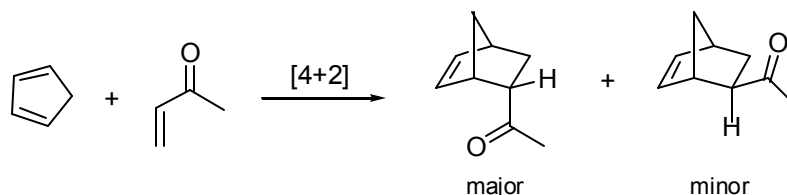
- In a cycloaddition reaction, two  $\pi$  systems react such that four  $\pi$  electrons go into forming two  $\sigma$  bonds to join the termini of the systems.
- The reaction will only proceed if the wavesigns match at the termini of the  $\pi$  systems

### Problem-Solving Approach

- Identify the two  $\pi$  systems (can be intramolecular)
- Sketch out the molecular orbitals for the systems
- Choose which system will serve as the HOMO and LUMO
- Regiochemistry and Stereochemistry: analyze both substituent perturbation and secondary interactions



- Cycloadditions will proceed only if the symmetries of the HOMO and LUMO are the same
- As discussed previously, substituents and Lewis acids catalysts will change the energies of the MOs. Anytime the relative energy of the HOMO and LUMO are changed, the reaction rate will also change. The closer they become in energy, the faster the reaction. The HOMO typically has electron donating substituents; the LUMO typically has electron withdrawing substituents.
- Endo selectivity can lead to the more sterically crowded product:



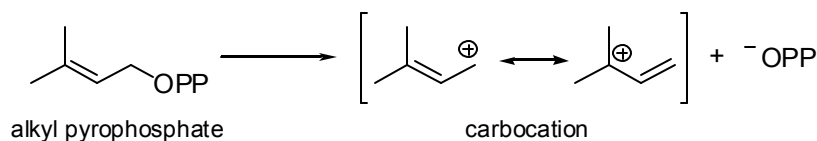
## Terpenoid/Carbocation Rearrangement Mechanisms

### General Notes

- I took this from a Chem 27 handout. Some of the material you don't know (yet). But, a fair amount of this stuff is applicable to this week's problem set.
- Enzymes often control the stereochemistry of these steps in a way that cannot be predicted "on paper."
- If faced with two plausible mechanisms, choose the alternative with the most stable intermediates and the fewest steps

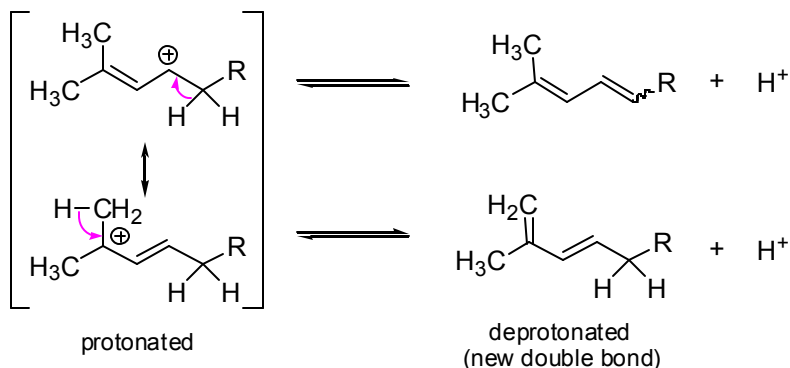
### Common Mechanistic Steps

#### 1) Ionization



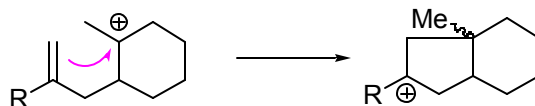
- Pyrophosphate ( $^-OPP$ ) is a good leaving group
- Loss of  $^-OPP$  results in the formation of a reactive carbocation

#### 2) Deprotonation



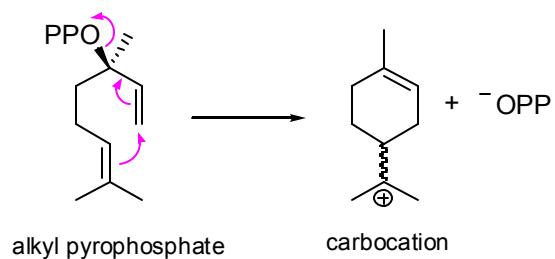
- Loss of a proton adjacent to a carbocation generates a double bond
- Always show protons being removed by a base (unlike the example above).

#### 3) Olefin Attack of a Carbocation



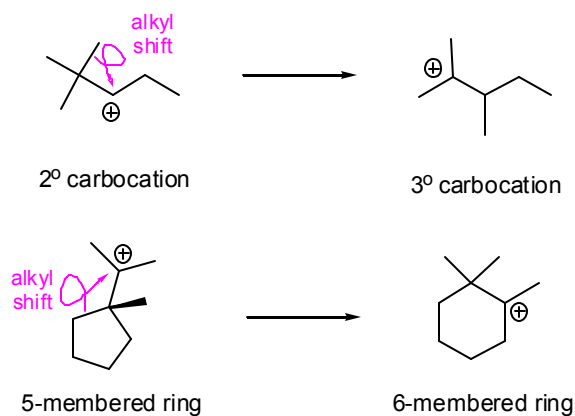
- The  $\pi$  bond is the nucleophile, while the carbocation (empty p orbital) is the electrophile
- Note that you are left with a new carbocation; the charge is conserved
- More often than not you attack with the less substituted carbon so that you generate the more substituted/stable carbocation

#### 4) S<sub>N</sub>2' Reaction



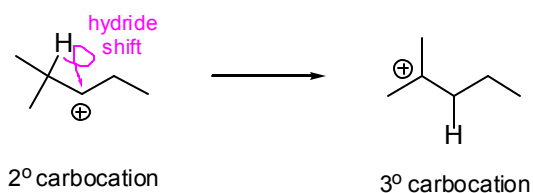
- The bottom  $\pi$  bond is the nucleophile, while the 3-carbon allyl system is the electrophile

#### 5) Alkyl Shift



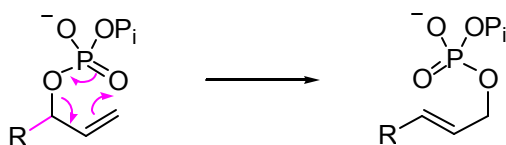
- Alkyl shifts are typically driven by the formation of a more stable cation
- Recall, carbocations are stabilized by greater alkyl substitution
- There is less ring strain in a six membered ring vs. a five membered ring

#### 6) Hydride Shifts



- Hydride shifts are also driven by the formation of a more stable cation

#### 7) Allyl-Phosphate Rearrangement



- This is a [3,3] sigmatropic shift, just like the Claisen rearrangement
- This is a key step in cases where, prior to phosphate rearrangement, the double bond is not positioned correctly to lead to a stable product (e.g., *trans* geometry)