UNIVERSITY OF DELAWARE

Chem 634

Pericyclic Reactions

Reading:
CS-B Chapter 6
Grossman Chapter 4

Pericyclic Reactions

Definition: Continuous, concerted reorganization of electrons

cyclic
transition
state

no intermediate,
single transition state

Bond breaking & bond making occur at the same time.

Can be synchronous (equal extent of breaking & making in TS) or asynchronous (unequal extent of breaking & making in TS).

Fukui & Hoffmann: Nobel Prize in Chemistry, 1981, “for… their theories, developed independently, concerning the course of chemical reactions” (Woodward dies in 1979)

5 Types

1. Electrocyclic
2. Cycloadditions
3. Sigmatropic
4. Chelatropic
5. Group Transfer

3 Theories

All 3 theories are correct!

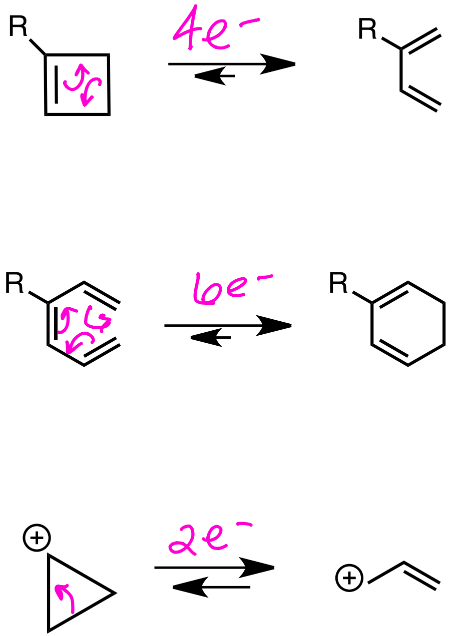
1. ***Woodward–Hoffmann***: Conservation of Orbital Symmetry
   - 1st historically
   - Uses *correlation diagrams*
2. ***Fukui***: Frontier Molecular Orbital Theory
   - Easier than Woodward–Hoffmann (usually)
   - Based on HOMO/LUMO interactions
3. ***Dewar–Zimmerman***: Aromatic Transition State
   - Easiest to apply for all reaction types, but not intuitive to understand why it's valid

3 Things Matter

1. Number of electrons involved
2. Stereospecificity
3. Conditions: heat (Δ) vs. light (*hυ)*

Type 1: Electrocyclic Reactions

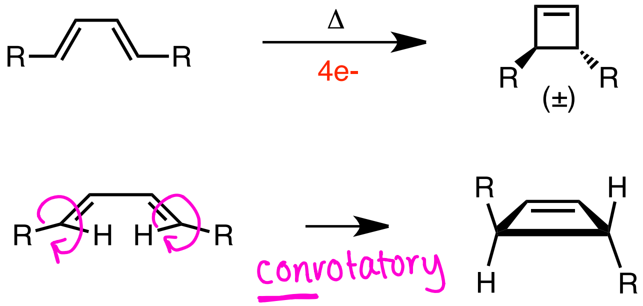
- Ring openings and closures
- Exchange π-bond for σ-bond
- Classified by number of electrons



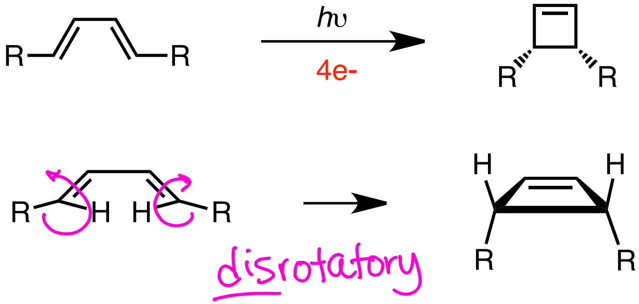
Double bonds
in conjugation
in SM or Pdt

Diastereoselectivity – Observations

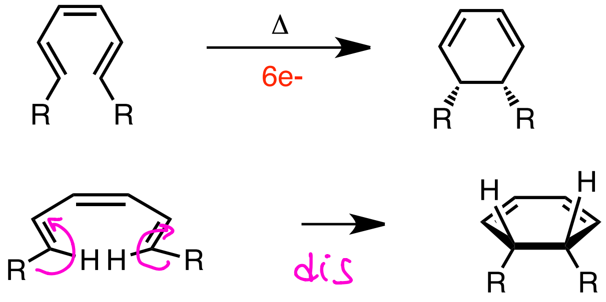
Case 1:



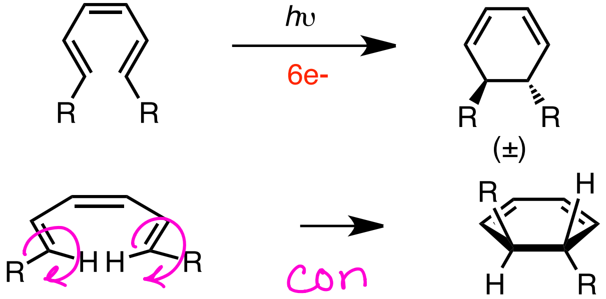
Case 2:



Case 3:



Case 4:



General Phenomenon… Woodward–Hoffmann Rules

Number of electrons	Thermal	Photochemical
4n	Con	Dis
4n+2	Dis	con

(n = integer)

6 points for a touchdown –> 6e-, thermal, disrotatory

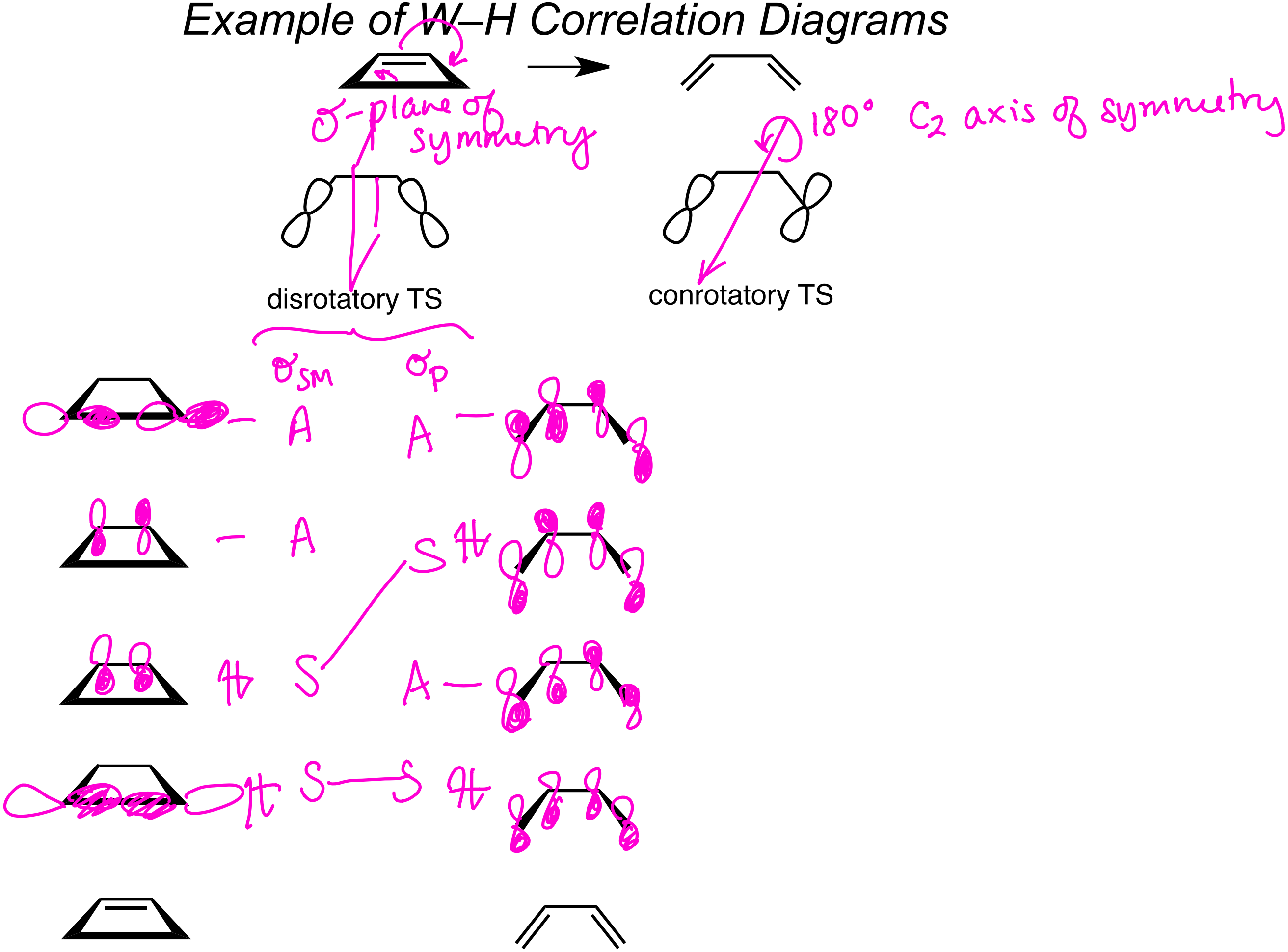
... But why???

Theory #1: Woodward–Hoffmann Correlation Diagrams

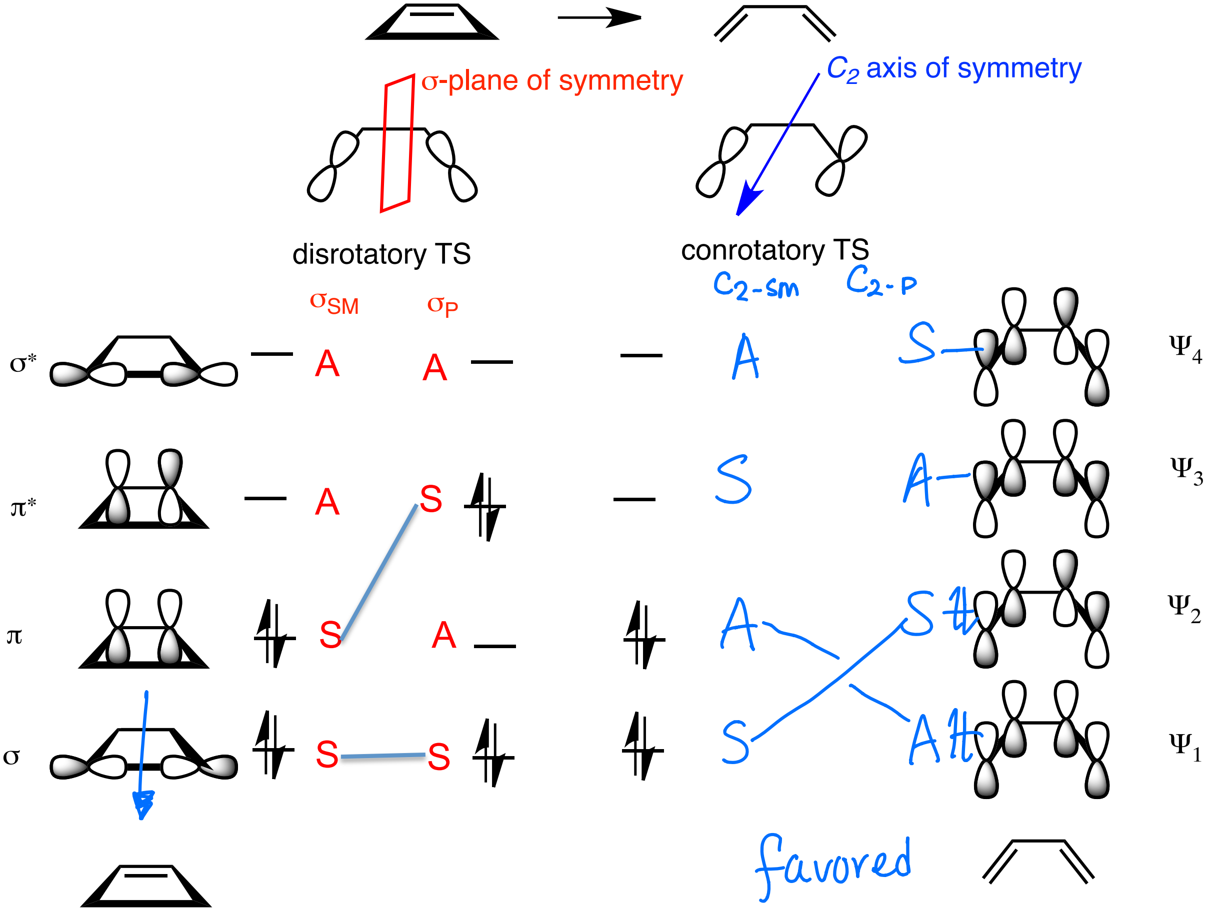
Angew. Chem. Int. Ed. **1969**, *8*, 781.

- Consider all molecular orbitals (MO's) involved
- Consider symmetry of MO's in starting material, product, *and transition state*.
- Orbitals of different symmetry can cross (orthogonal orbitals).
- Orbitals of same symmetry *cannot* cross (extreme energetic cost).
- We are about orbitals where electrons end up.

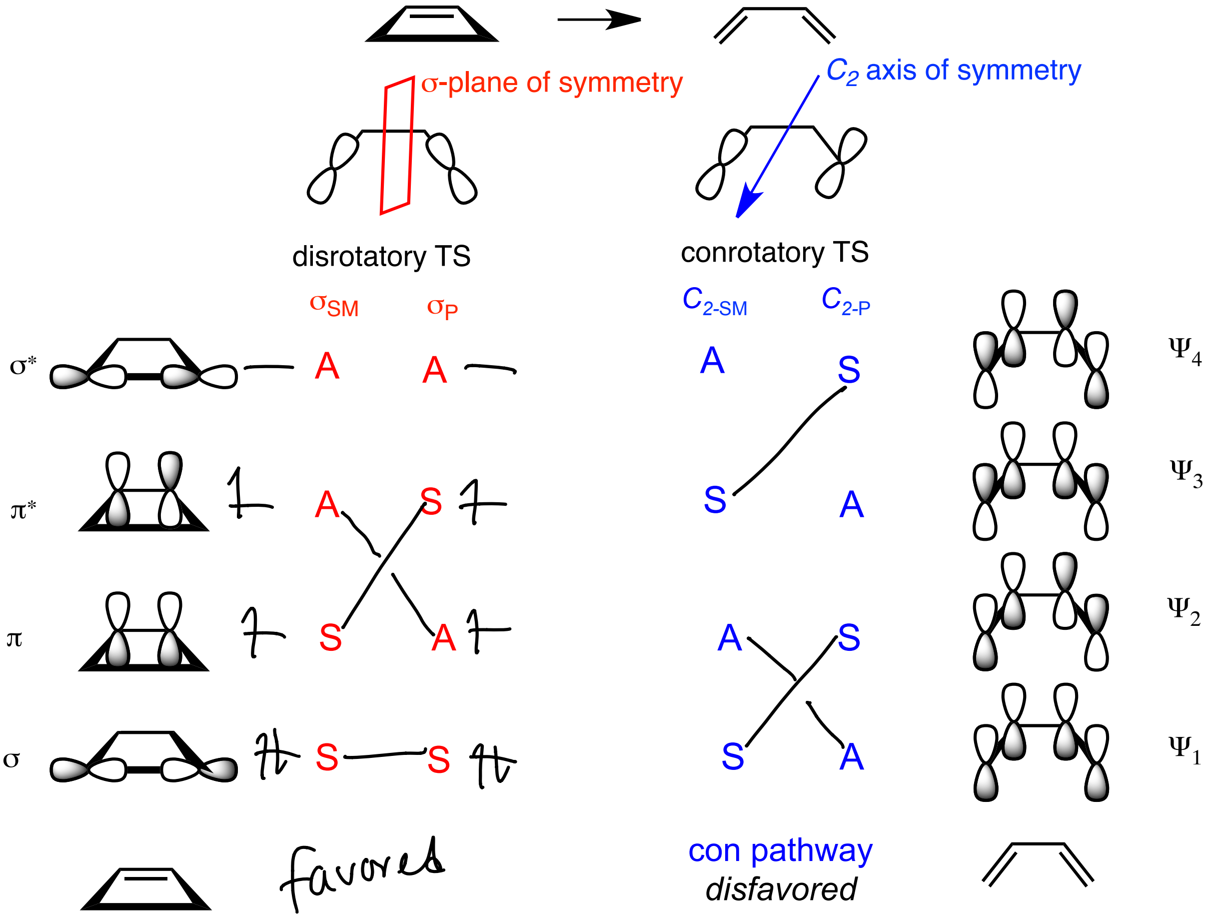
Example of W–H Correlation Diagrams



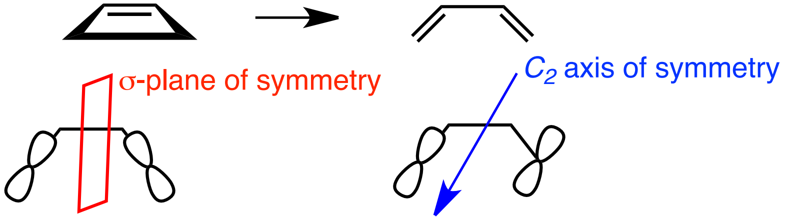
Example of W–H Correlation Diagrams: Thermal Conditions



Example of W–H Correlation Diagrams: Photochemical Conditions

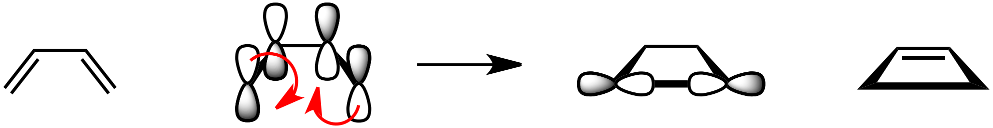


W–H Conservation of Orbital Symmetry Shortcut



disrotatory TS

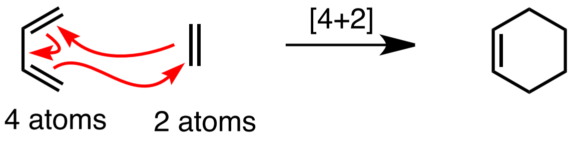
conrotatory TS



Ψ_2
(HOMO)

Cycloadditions & Cycloreversions

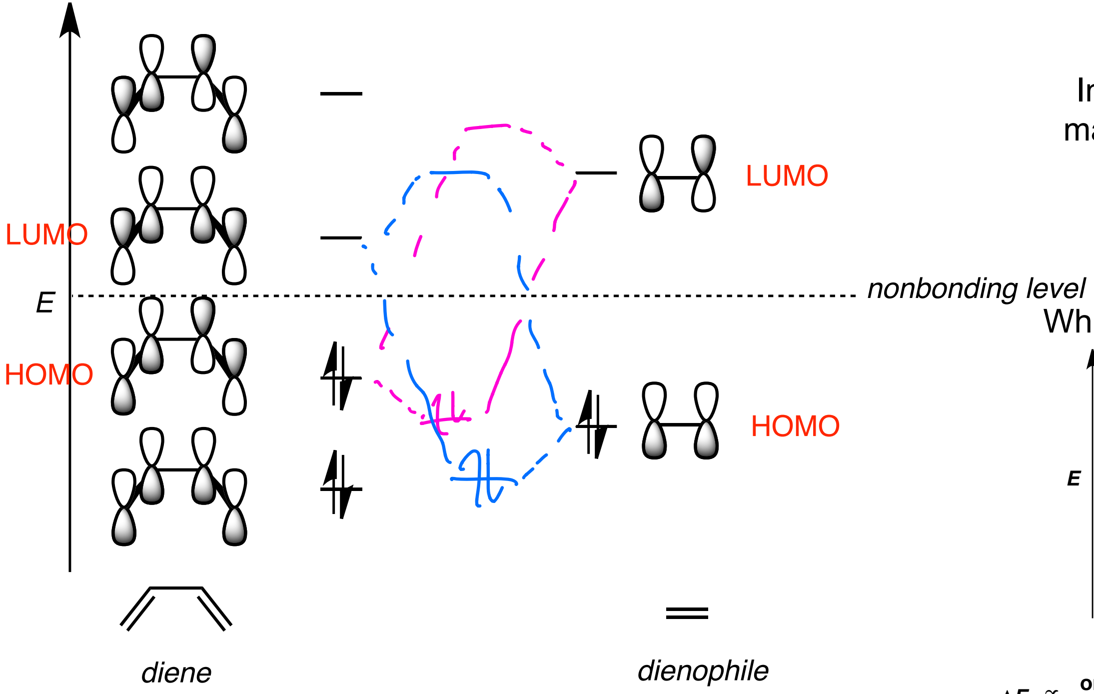
- Union of 2 π-systems
- Exchange π-bonds for σ-bonds
- Classified by [m+n], m & n = # of conjugated *atoms* in each π-system



Diels–Alder Reaction!
Note: 6 e-
Great way to make cyclohexenes & cyclohexanes

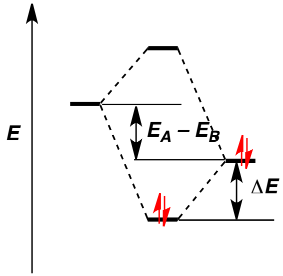
Fukui: Frontier Molecular Orbital (FMO) Theory

The idea: Use FMO's (HOMO + LUMO)



In this case, it doesn't matter… HOMO/LUMO gaps are the same.

Which HOMO & LUMO?



$$\Delta E \propto \frac{\text{orbital overlap}}{E_A - E_B}$$

geometrical/spatial overlap

If closer in energy, then more stability by forming a covalent bond.

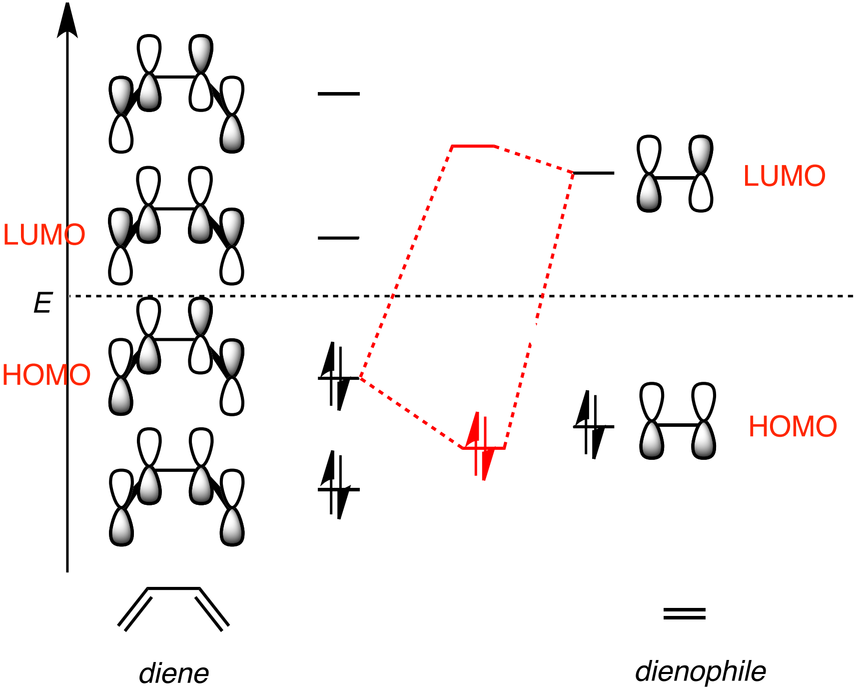
Types of Diels–Alder Reactions

Normal electron demand = HOMO of diene + LUMO of dienophile

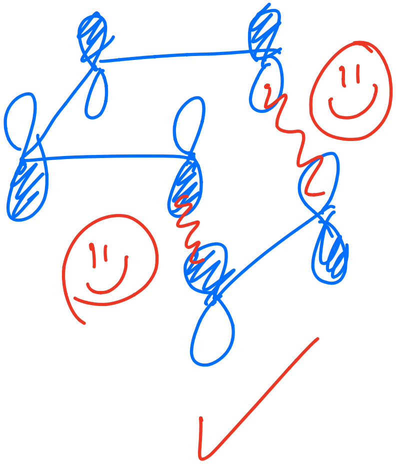
Inverse electron demand = HOMO of dienophile + LUMO of diene

Net Bonding Interaction?

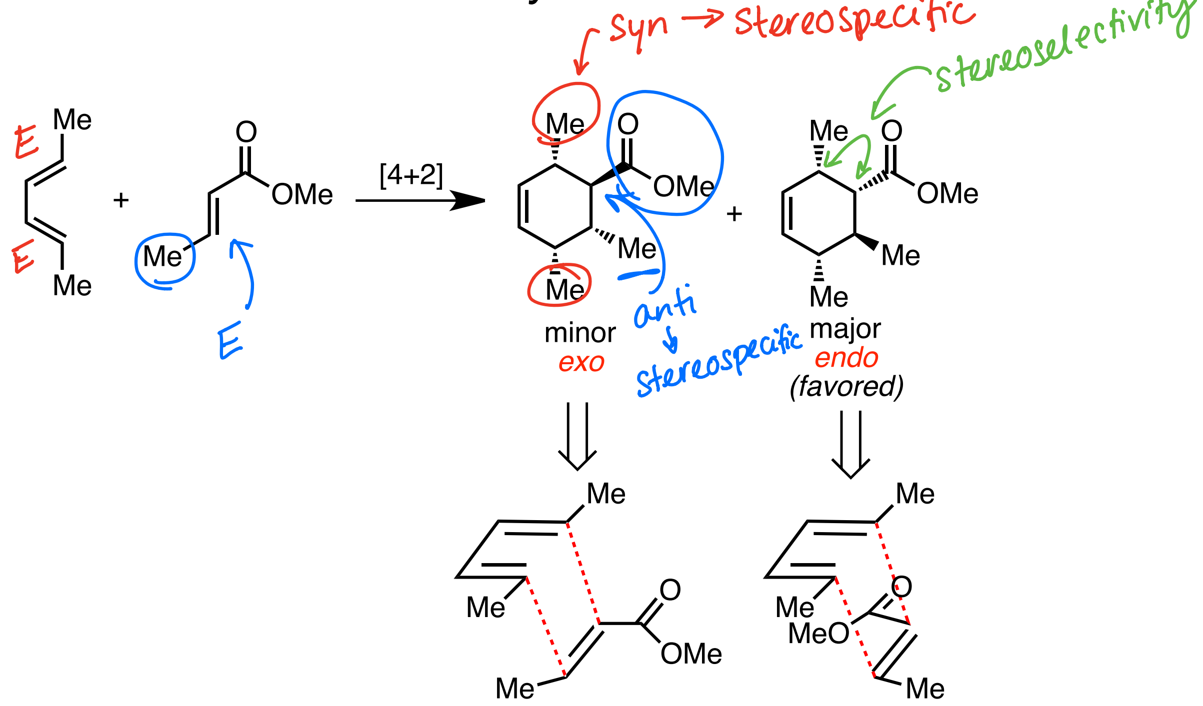
The idea: Use FMO's (HOMO + LUMO)



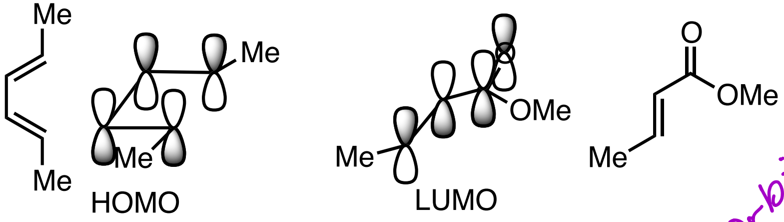
nonbonding level



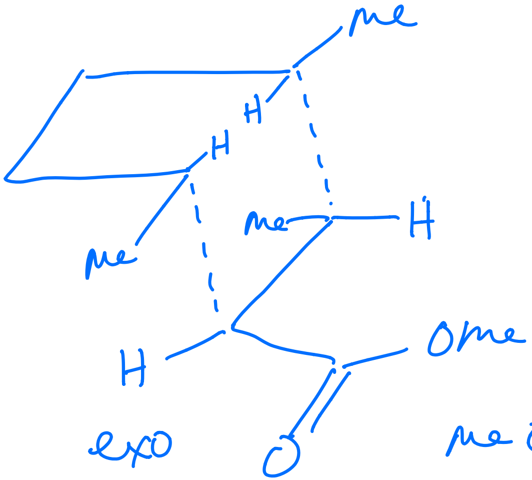
Diastereoselectivity: Endo vs. Exo

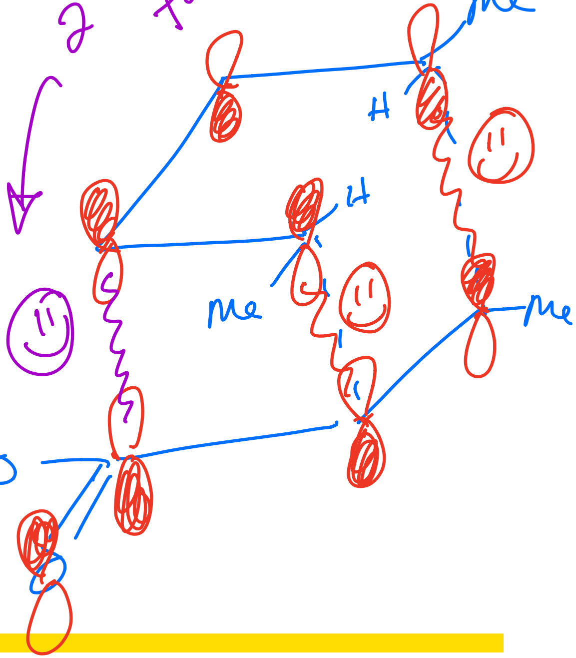


Why? … Secondary Orbital Interactions



2° Orbital Interaction
favors endo



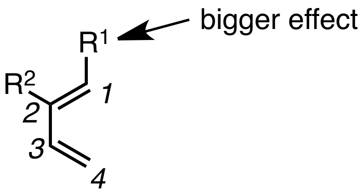


Regioselectivity & Rates: Substituent Effects

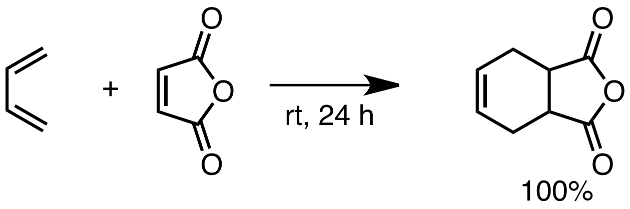
Rates depend on HOMO/LUMO gap.

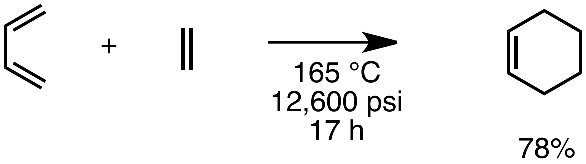
	Perturbation	HOMO	LUMO
Ph	extra conjugation	↑	↓
$\xi-\overset{\overset{O}{\|}}{C}-R$	electron-withdrawing group	↓	↓
$MeO-\xi$	electron-donating group	↑	↑

Effects apply to both dienes & dienophiles.
Effect of substitution is biggest if on C1 of diene.



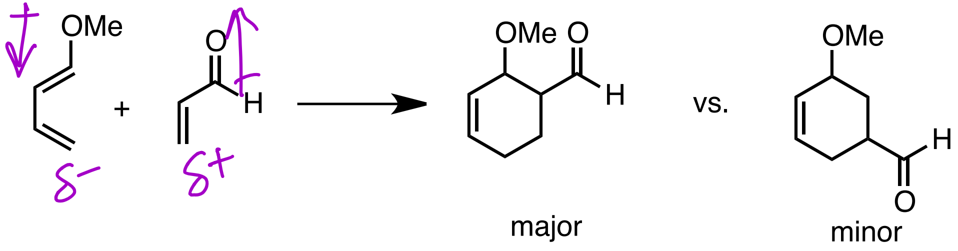
Examples



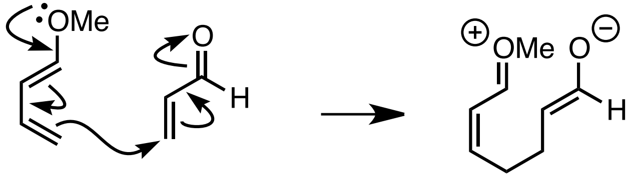


Regioselectivity

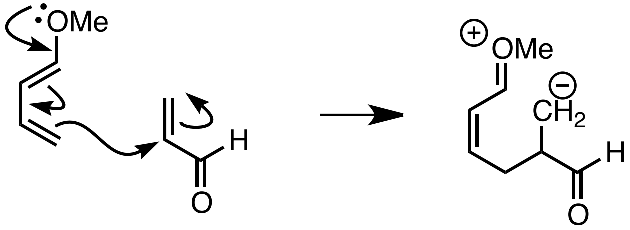
Related to polarization of HOMO and/or LUMO



Quick prediction: “imaginary intermediate”
(push arrows to get maximum effect of substituents)



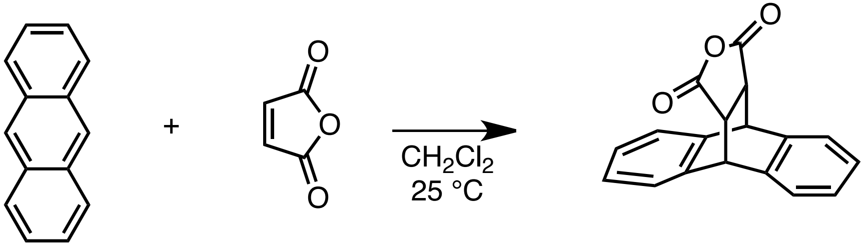
more stable



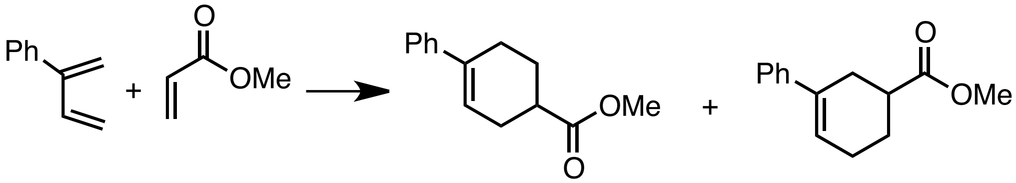
… but remember these reactions are *concerted*!!!

Lewis Acid Effects

One of the first Lewis acid-accelerated organic transformations!



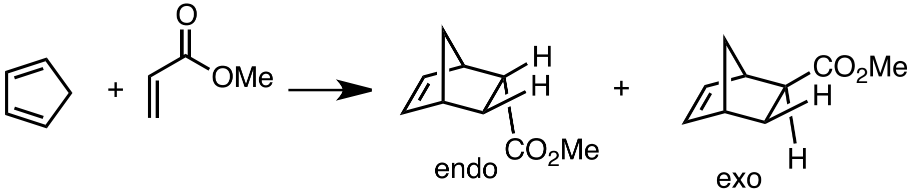
additive	$t_{1/2}$
none	2400 h
$AlCl_3$ (1 equiv)	< 1 min



1,4

1,3

additive	1,4 : 1,3
none	80 : 20
$AlCl_3$	97 : 3



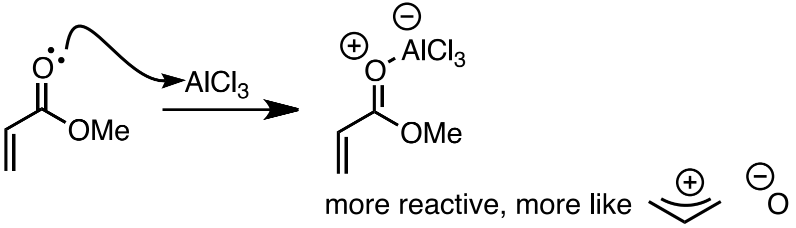
additive	endo:exo
none	82 : 18
$AlCl_3 \cdot OEt_2$ (1 equiv)	99 : 1

Lewis acid increases rate, endo/exo selectivity & regioselectivity!

Yates, Eaton. *JACS* **1960**, *82*, 4436

Why???

MO perturbation!



more reactive, more like

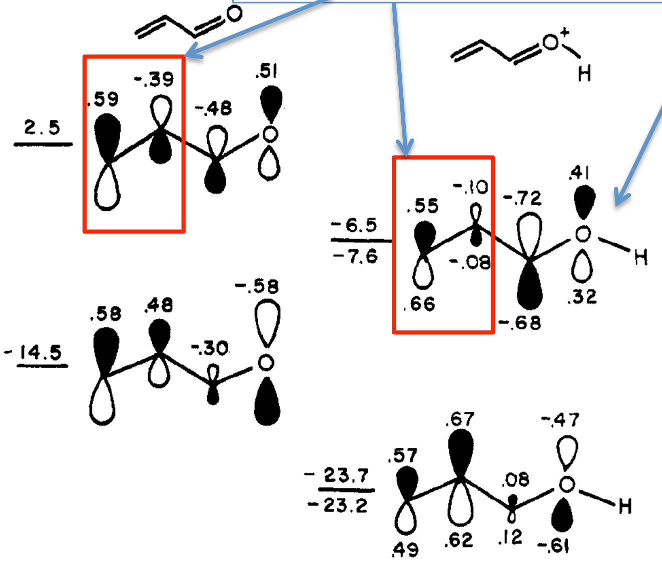
Explains rates, but what about selectivity issues???

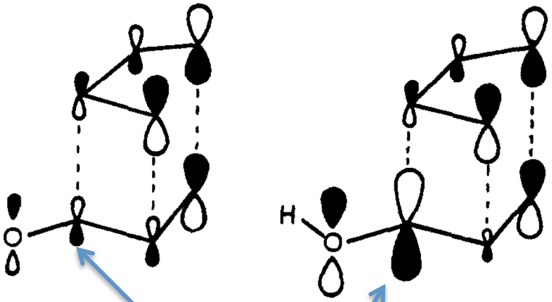
Houk *JACS* **1973**, *95*, 4094

Why???

Bigger difference in lobe size on C1 vs. C2 = better regioselectivity

Lower LUMO = faster rate

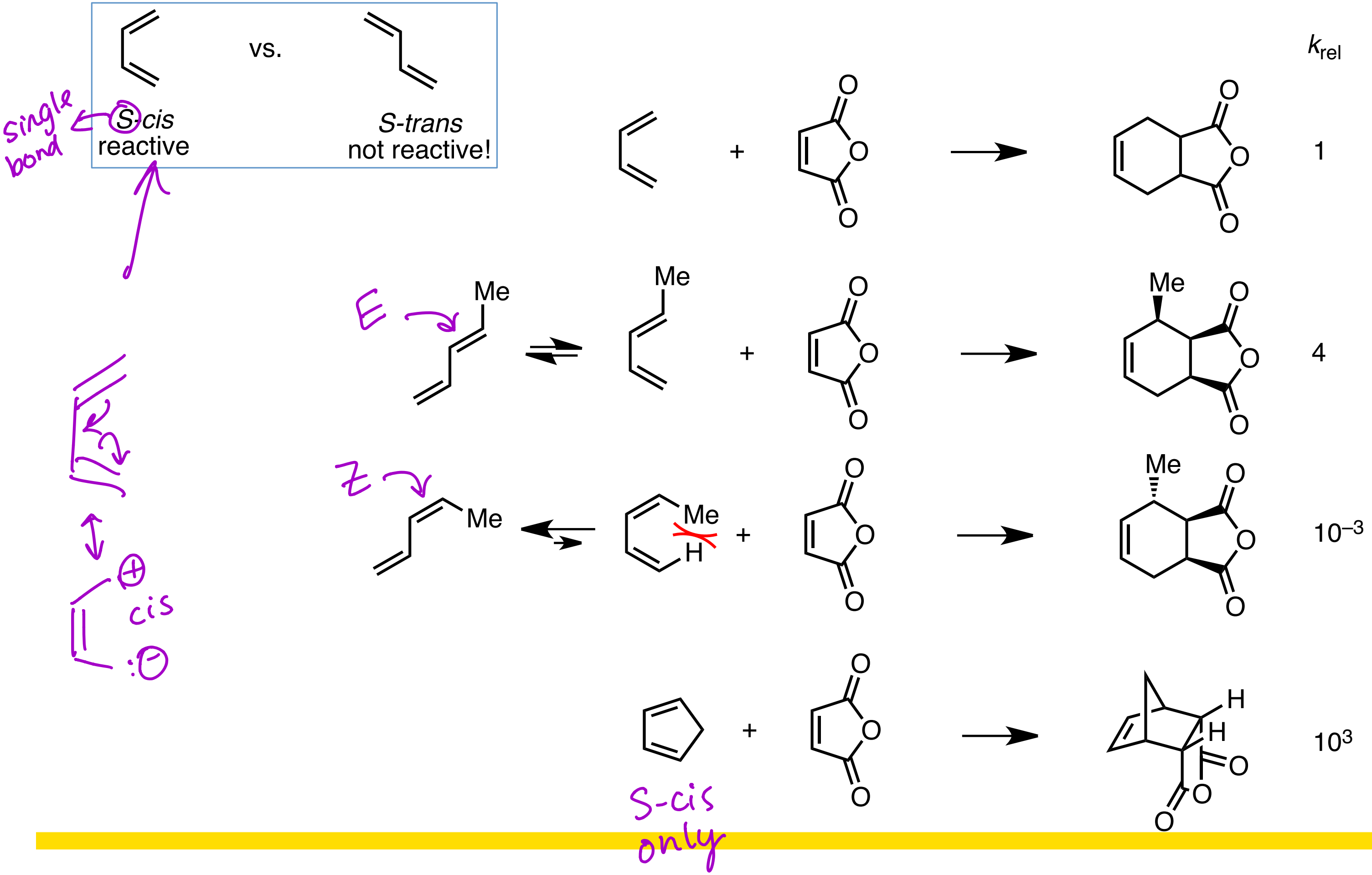




Bigger lobe on C=O carbon = bigger 2° orbital interactions = better endo/exo selectivity

Houk *JACS* **1973**, *95*, 4094

One More Consideration: S-cis vs. S-trans



S-cis reactive

vs.

S-trans not reactive!

single bond

k_{rel}

1

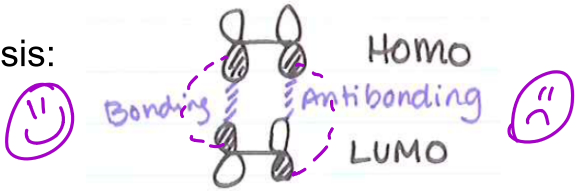
4

10^{-3}

10^{3}

[2+2] Cycloadditions

FMO Analysis:

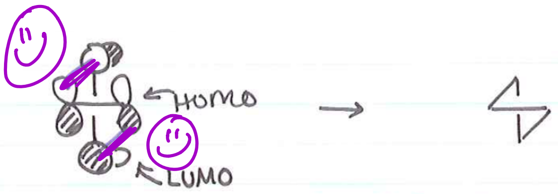


- No net bonding… "forbidden"
- This geometry is *suprafacial* on both π bonds => $[2\pi_s + 2\pi_s]$

Suprafacial = same face of π-system

Antarafacial = opposite faces of π-system

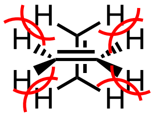
Alternative Transition State Geometry



Net bonding!

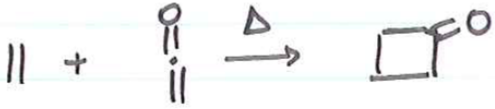
SUPRAFACIAL ON LUMO
ANTARAFACIAL ON HOMO } $[2\pi_s + 2\pi_a]$ ALLOWED!

Problem: Steric Hindrance!



Solution: Remove steric hindrance!

(allene)



ketene

Sigmatropic Reactions

- Reorganization of σ and π bonds (migration of a σ-bond)
- Number of σ and π bonds remains constant
- Classify by [m,n]-rearrangement or [m,n]-shift (m, n = number of atoms in fragment)

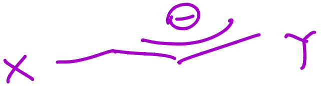
[1,3]-Sigmatropic Rearrangement

Does this rearrangement proceed under thermal conditions?

Supra- or antara-facial??

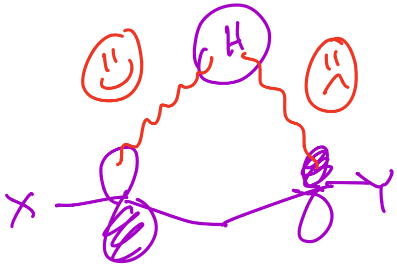
For FMO, break into HOMO and LUMO:

$H^{\oplus}$ ← LUMO



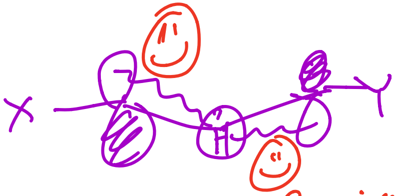
← HOMO

+



Suprafacial on allyl } Forbidden

But too far!

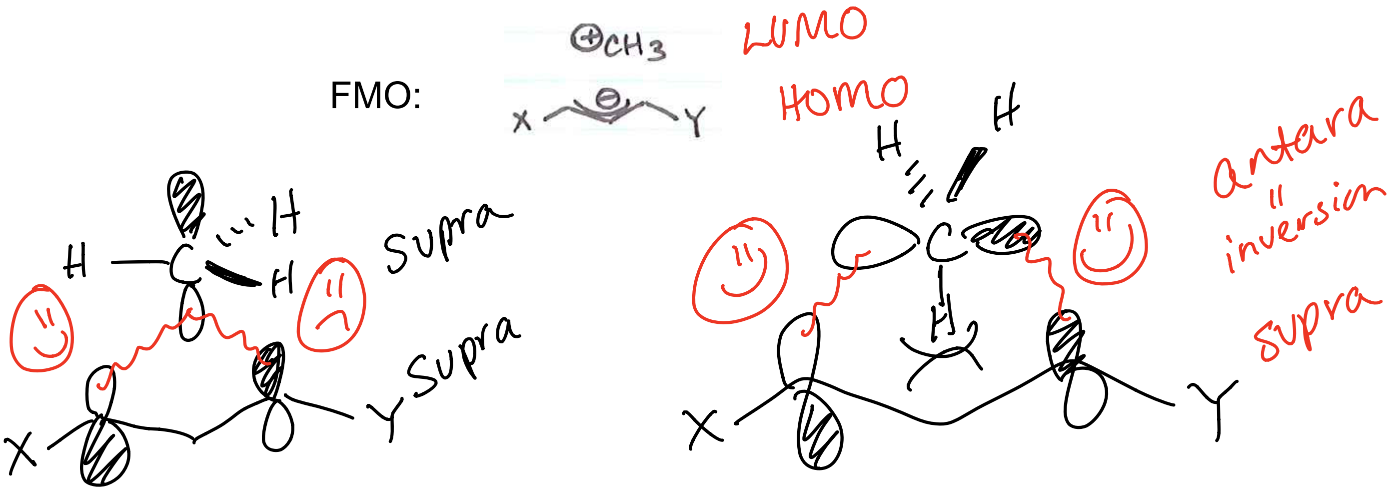


antarafacial on allyl } Allowed

[1,3]-Sigmatropic Rearrangements

Alkyl Shift?

FMO:



Forbidden

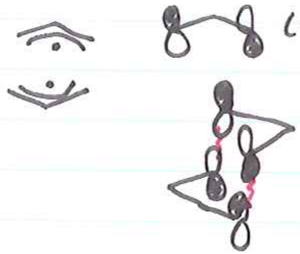
Strained → rare

[3,3]-Sigmatropic Rearrangements

Cope, as drawn ΔG = 0

FMO Analysis:

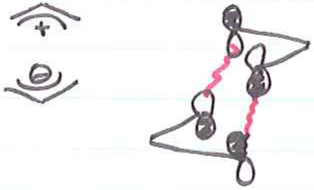
2 Allyl radicals:



2 bonding interactions

or

Allyl cation & anion



Suprafacial on both components!

Highly predictable TS –> “chair-like” (can predict stereochem)

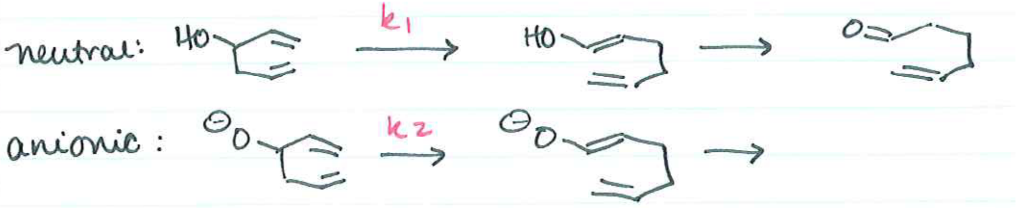
Claisen Rearrangement

$\Delta G < 0$

C–O π > C–C π

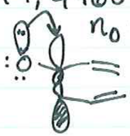
Oxy-Cope

2) Tautomerization of Pdt: Oxy-Cope.



$\frac{k_2}{k_1} = 10^{10} - 10^{17}$!! JACS 1975, 97, 4765.

Why? Ground-state destabilization
&
TS-stabilization



$n_O \rightarrow \sigma^*_{C-C}$ { weakens C-C bond.

stabilizes radical character on allyl fragment

⇒ Asynchronous (bond breaks more than bond forms in TS)

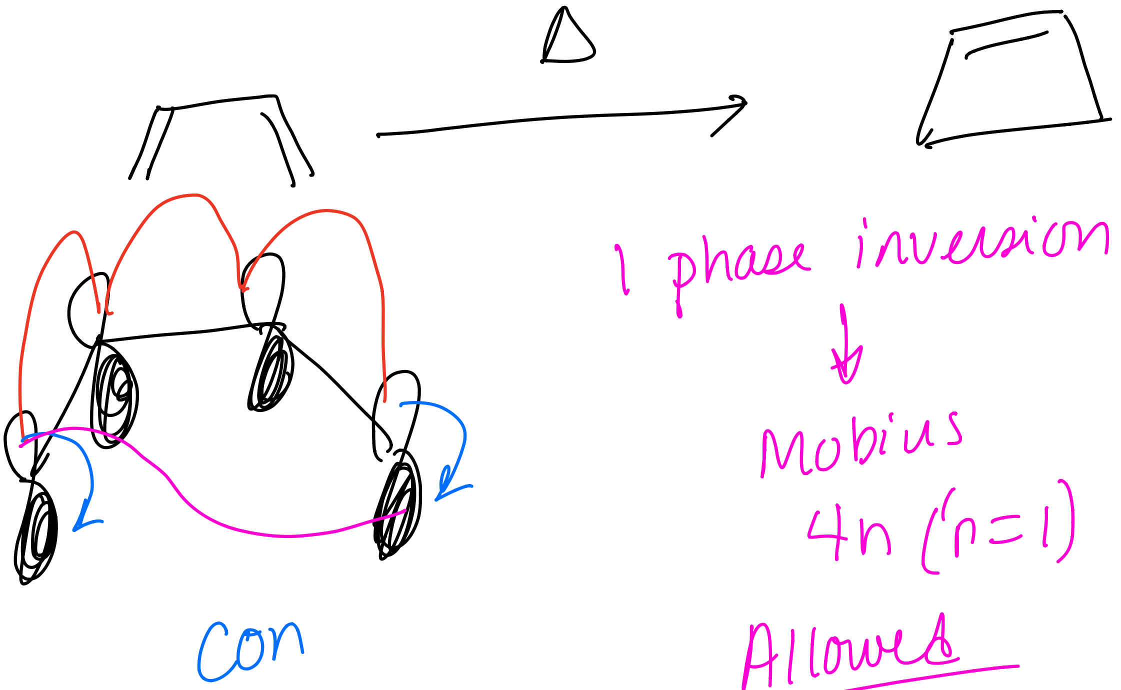
Theory #3: Dewar–Zimmerman: Aromatic Transition State

Steps:

1. Choose basis set of 2p AO's (or 1s for H atoms)
2. Assign phases (any phases)
3. Connect orbitals that interact in the starting material
4. Connect lobes that begin to interact in the reaction
5. Count the number of phase inversions
6. Identify topology
   1. Odd # of phase inversions = Möbius
   2. Even # of phase inversions = Hückel
7. Assign Transition State as *aromatic* (thermally allowed) or *antiaromatic* (photochemically allowed)

System/Topology	Aromatic	Antiaromatic
Huckel	(4n+2) e-	(4n) e-
Mobius	(4n) e-	(4n+2) e-

Example of D–Z Theory



1 phase inversion

↓

Mobius

4n (n=1)

Allowed