Lecture VIII: Pericyclic Reactions, Cycloadditions

02/05/2010

1. Aromatic TS theory
2. More nomenclature
3. [4+2] Cycloadditions
   - Electronics
   - Selectivity

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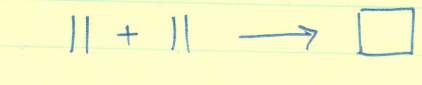
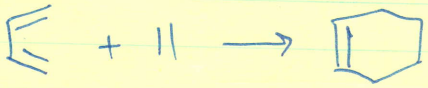
① Theory of aromatic transition states (Evans/Zimmerman) is the final method of interpreting pericyclic reactions:

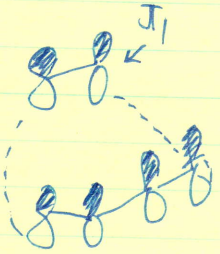


4 π-electrons — $4n$ pseudoantiaromatic — FORBIDDEN



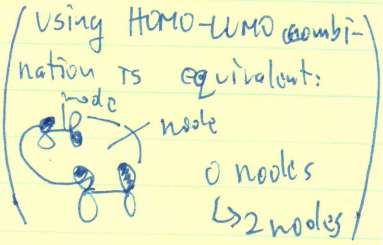
6 π-electrons — $4n+2$ pseudoaromatic — ALLOWED

↳ 10 π electrons is good too—remember the [6+4]?

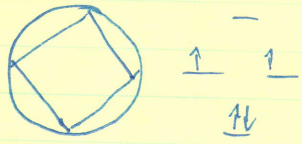


6π-electrons
favorable

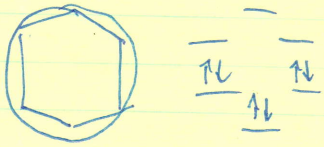
4π-electrons
unfavorable



The way they are drawn, these TSs have 0 nodes, and are called classical "Hückel" aromatic/antiaromatic systems:

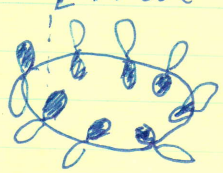


bad



good

However, things change if there is a twist in the system! If there's a twist in the array of π-orbitals, we talk about a Möbius system:



one-node (or odd-node) Möbius type system!

For Möbius system, HMO inverts the aromaticity rules:

$4n$ – good aromatic

$4n+2$ – bad antiaromatic

WRONG SYMMETRY

or

4π-Hückel

} both BAD, but =>

Works, with a twist!
Möbius 4π – OK!

Möbius aromaticity recently was observed in neutral stable molecules too – this was a challenge because of the need for a twist.
Review: Nature Chem, 2009, 1, 113-122
Nature 2003, 426, 819 – first example

(2) More nomenclature – book-keeping

When describing a pericyclic reaction, we need to account for:

a) Number of electrons:

[4+2], [2+2], [6+4]
↳ can be π or σ bonds, or lone pairs (ω)

More precisely, D-A rxn is $[_{\pi}4 + _{\pi}2]$

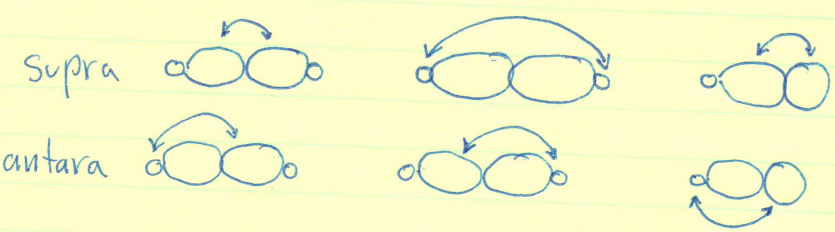
b) Stereochemistry of attack:

SUPRAFACIAL
two new bonds formed on the same side of the system

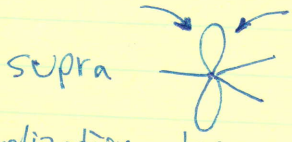
ANTARAFACIAL
new bonds formed on opposite sides

π:

σ:



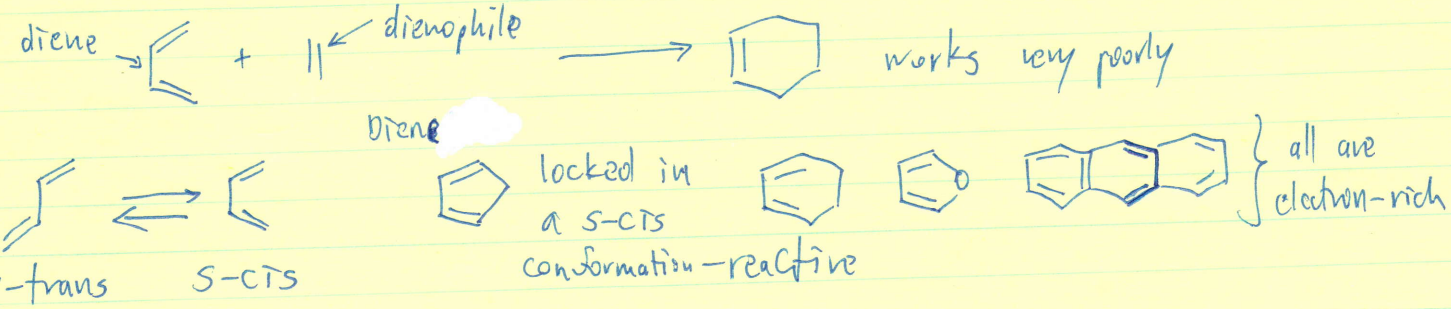
For free electron pairs (ω):



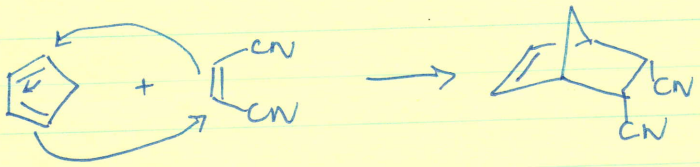
Diels-Alder
$[_{\pi}4_s + _{\pi}2_s]$

In electrocyclizations, terms "conrotatory" and "disrotatory" are often used, but they are superfluous.

(3) [4+2] Cycloadditions – Diels/Alder reactions



Electron-poor dienophiles:



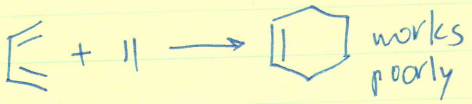
this electron-pushing is a formality and is probably wrong, in terms of representing the course of the reaction. Works for describing the connectivity

Diels-Alder is $[_{\pi}4s + _{\pi}2s]$, allowed, a+a would be allowed also
s+a/a+s would be forbidden, because of Mobius geometry

Experimental observations

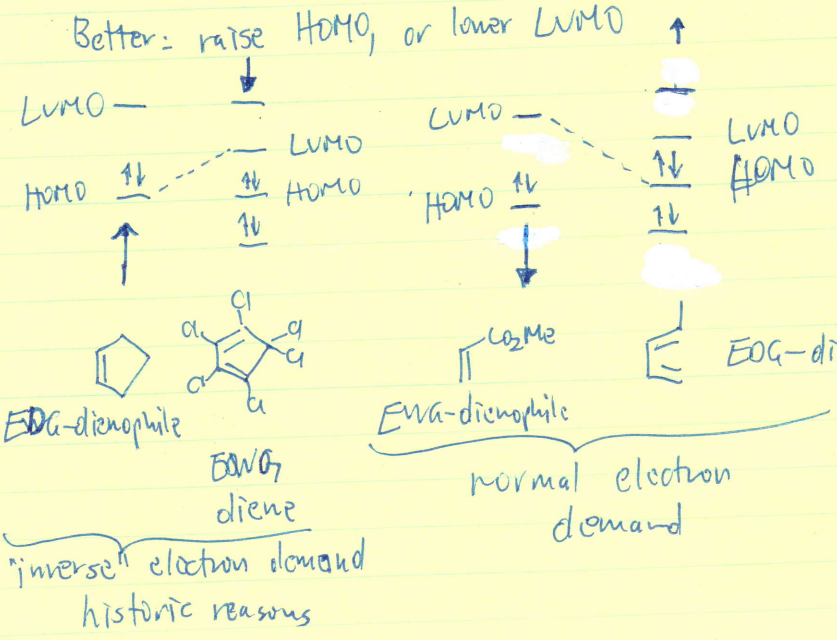
- 2nd order, as expected
- little solvent dependence (no ionic species)
- inverse 2° KIE ($sp^2 \rightarrow sp^3$)
- pressure helps (products have smaller volume)
- negative entropy of activation (highly ordered TS)
- H_2O helps, because it brings reactants closer ⇓ hydrophobic effect

Substituent Effects

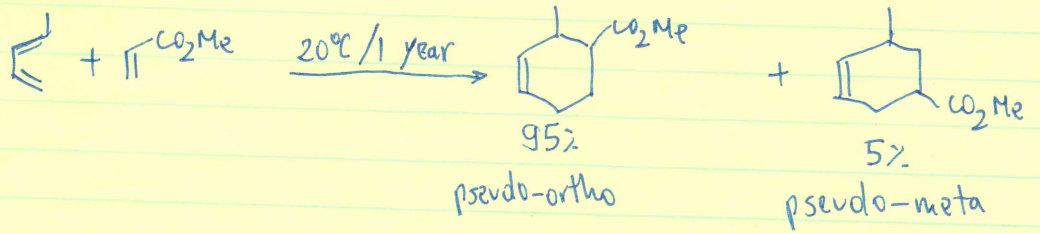


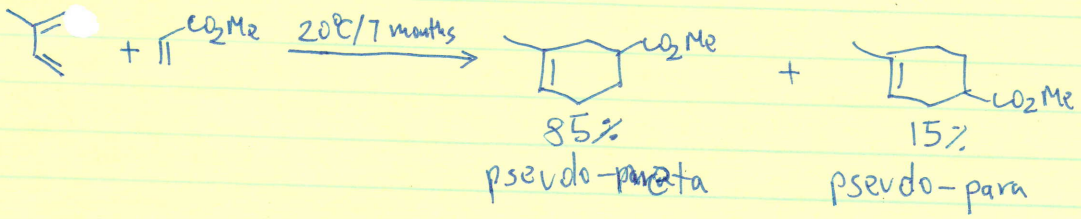
This analysis also explains the positive effect of added Lewis acids on the rxn rate, as they further lower the LUMO of the EWG-substituted dienophiles.

Better: raise HOMO, or lower LUMO

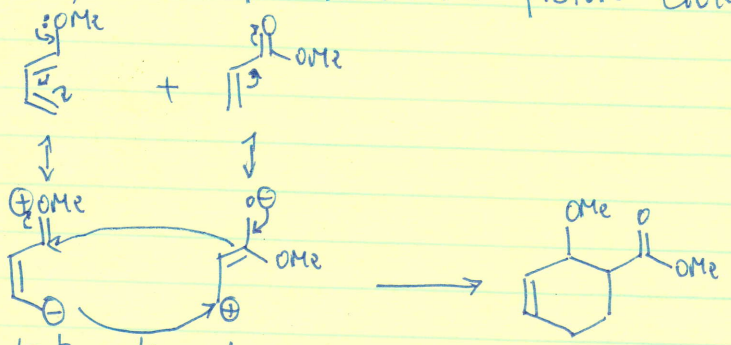


Selectivity in Diels-Alder reactions



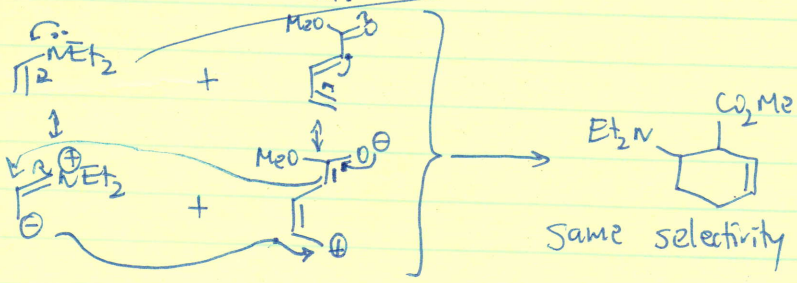


For pseudo-ortho, a simple resonance picture could work:

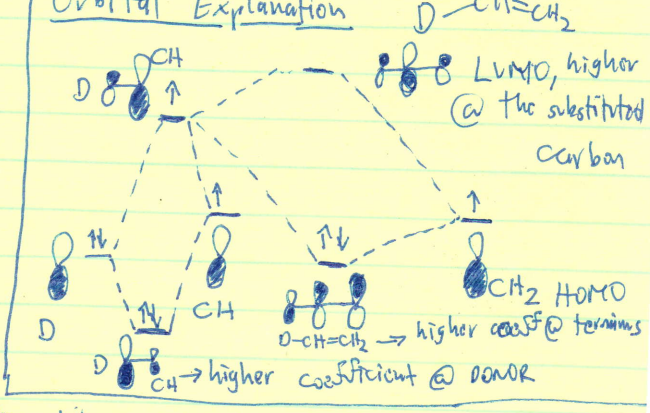


this is NOT the actual mechanism!

For inverse electron-demand:



Orbital Explanation



The coefficient for both HOMO and LUMO (for diene and dienophile) can be easily calculated.

Stereoselectivity - very powerful, forms 4 contiguous stereocenters in a highly organized fashion: